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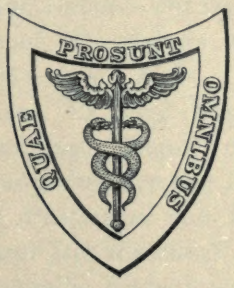
EDITED BY

FRANCIS R. PACKARD, M.D.

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THE

AMERICAN JOURNAL

OF THE MEDICAL SCIENCES.

JANUARY, 1903.

SARCOMA OF THE THIRD CERVICAL SEGMENT: OPERATION; REMOVAL; CONTINUED IMPROVEMENT.[1]

By James W. Putnam, M.D.,

PROFESSOR OF NERVOUS DISEASES, MEDICAL DEPARTMENT, UNIVERSITY OF BUFFALO; CONSULTING NEUROLOGIST, BUFFALO GENERAL HOSPITAL,

AND

William C. Krauss, M.D.,

CONSULTING NEUROLOGIST, BUFFALO GENERAL HOSPITAL.

WITH A SURGICAL REPORT

By Roswell Park, A.M., M.D., LL.D.,

PROFESSOR OF SURGERY, MEDICAL DEPARTMENT, UNIVERSITY OF BUFFALO; SURGEON TO THE BUFFALO GENERAL HOSPITAL.

The literature on spinal cord tumors with operation begins with the epoch-making case of Horsley and Gowers in 1888, although Leyden in 1874 and Erb again in 1878 urged surgical procedure in cases where the diagnosis could be safely established. The high standing of the English neurologist, Sir William Gowers,[2] an honorary member of the Association; the accuracy of the diagnosis; the keenness and certainty of the surgeon's skill, and the brilliancy of the results obtained in this first operation attracted others to this most important field, so that Starr,[3] in June, 1895, was able to collect 22 cases of spinal cord tumors, with operations. Of these 22 the tumor was successfully removed in 13, while death followed the operation in 9. Of the successful operations, a recovery from the condition of paraplegia occurred

[1] Read at the Twenty-eighth Annual Meeting of the American Neurological Association held at New York, June 5, 6, and 7, 1902.

[2] Med. Chirurg. Trans., 1888, p. 407.

[3] The American Journal of the Medical Sciences, June, 1895, p. 613.

in 6. In explanation of the unfavorable results, Starr well says that an operation has not been undertaken until the tumor has been going on for a number of months, and until the secondary destruction of the spinal cord tissues was of such a nature that a regeneration of the nerve elements was practically out of the question.

Bruns, in 1898, collected 20 unquestioned cases of spinal tumor, with operation. In 18 of the 20 cases the correctly diagnosed tumor was removed during the operation; in 1 instance it was not found because the opening was made too low, and in another case because it was a flat sarcoma of the meninges, which was not recognized during the operation. In 6 of these 20 cases marked improvement and even recovery was attained—that is, exactly 30 per cent.; in 2 only very slight and in 1 temporary improvement followed. In 12 cases death occurred—9 soon after operation, by shock after hemorrhage and sepsis; 3 at a later date, by relapse, marasmus, and extension of the tumor, which was not discovered during the operation.

Of these 20 cases, in 14 the tumor was located in the thoracic region, 2 in the lumbar, 2 in the sacral, and 1 in the cervical. The nature of the tumor removed was sarcoma in 9, psammoma in 2, and 1 each of fibromyxoma, lipoma, endothelioma, echinococcus, lymphangioma, tubercle, and in 3 not stated. The tumor was found to be extradural in 11 cases, intradural in 7, and not stated in 2.

The next notable addition to the literature on the subject was made by Putnam and Warren,[1] of Boston, in 1899. They reported 33 cases of tumor with operation. Of these 7 led to recovery and 10 to more or less improvement, although only in 5 of these latter was the improvement considerable or lasting. The neoplasms removed in the satisfactory cases were fibroma in 3 cases, echinococcus in 2, and 1 each of lipoma, psammoma, and sarcoma.

In 10, perhaps 12 cases, operation seems to have hastened death, while in 9 the operation seems to have made little difference in the progress of the case. The location of the tumor in these cases was: extradural, 20; intradural, 7; intradural and extradural, 1; intramedullary, 1; not stated, 4. The nature of the tumor was sarcoma in 14, echinococcus in 5, fibroma in 2, psammoma in 2, and 1 each of endothelioma, cancer, fibromyxoma, chondrosarcoma, lipoma, lymphangioma, and tumor of the vertebra. The tumor was located in the thoracic region in 25 cases, 2 in the lumbar region, 1 in the sacral, 1 in the cervical, 1 in the thoracic and lumbar, 1 in lumbar and sacral, and 2 not stated.

The next classified list of spinal cord tumors with operation to appear in the current literature is that of Samuel Lloyd's, published in the

[1] The American Journal of the Medical Sciences, October, 1899.

Philadelphia Medical Journal, February 22, 1902. The list is incomplete, as it does not contain the case of Starr and McCosh,[1] published in the *Journal of the American Medical Association*, August 31, 1901; nor Oppenheim's case, published in the *Berliner klinische Wochenschrift*, January 13, 1902; nor Fedor Krause's case, published in the *Berliner klinische Wochenschrift*, June 3, 1901. The list includes some cases not properly belonging to spinal cord tumors.

Lloyd included 51 cases in his list. Of these 16 recovered, or 31.37 per cent.; 4 improved, 2 were unimproved, and 5 died immediately and 23 some time after the operation.

The location of the tumor was as follows: extradural, 29; intradural, 10; intravertebral, 10; extravertebral, 14; not stated, 3. The nature of the tumor was sarcoma in 15 cases, echinococcus in 8, lipoma in 3; cancer, abscess, fibroma, lymphangioma, psammoma in 2 each; myxosarcoma, myxoma, chondrosarcoma, osteosarcoma, enchondroma in 1 each, and in 10 not stated. The tumor was located 37 times in the thoracic region, 7 in the lumbar, 2 in the cervical, 1 in the sacral, and not stated in 2.

From a study of these different collections the sarcoma is by far the most common tumor affecting the spinal cord. It was found present in 45 per cent. in Bruns', 42 per cent. in Putnam's, and in 29.4 per cent. of Lloyd's cases. The most frequented portion seems to be the thoracic region, while the cervical is the least frequented. In situation the extradural is much more prevalent than the intradural, while the intramedullary is extremely rare.

The percentage of recovery in Bruns' and Lloyd's collection is practically the same, being 30 per cent. in the former and 31.37 per cent. in the latter. In Putnam and Warren's collection the percentage is lower, being 21.2 per cent., while the percentage of improvement is also 21.2 per cent. The history of the case which we desire to place on record is as follows:

April 2, 1902, Dr. Putnam was called to see the patient, J. E., and obtained the following history: Male, aged forty-five years; married, but has no children; habits temperate. Previous history of good health all his life and freedom from any serious accidents; no falls upon the back. In the autumn of 1900 he complained of occasional sudden, sharp attacks of pain. These would begin in the back of the neck and radiate around the neck and up the occiput. The pains would last from two to five minutes, during which time he says he suffered most intense agony. He would grasp a chair in front of him and hang on, but, in spite of himself, he would be forced to yell and scream with pain. He says that on two occasions he lost consciousness, and he would frequently have dizzy attacks. During the first few months the intervals of freedom from pain were often a week, but

[1] Starr, M. Allen. Philadelphia Medical Journal, February 8, 1902.

gradually the intervals shortened, until he would have them several times daily. In addition to the symptoms of periodical pain he suffered from some constipation and from difficulty in fully emptying the bladder. In the spring of 1901 he went to California, and later to Hot Springs, Ark., believing that he was suffering from rheumatism. His best recollection is that he had a sensation of numbness in the left hand in the spring of 1901, and that was followed by weakness of the muscles of the left hand and arm. The right hand was affected with numbness and weakness some months later. The legs were affected with weakness and disturbed sensation in December, 1901; he was, however, able to walk until the early part of February, 1902. From March until April 2d the symptoms increased. Examination by Dr. Putnam at that time revealed the following conditions:

Reflexes of flexors and extensors of forearms and of biceps and triceps very much exaggerated.

Reflexes of abdominal muscles and cremasteric reflex exaggerated; knee-jerks and ankle clonus and patellar clonus were very marked. Babinksi reflex present. There was a large bed-sore over the sacrum. There was no other trophic disturbance. There was no control over the bowels and bladder. Bowels were constipated and urine was voided involuntarily. There was total loss of sensation from the clavicle down, this being tested with an æsthesiometer and with heat and cold. Motion was entirely lost in the muscles of the left arm and leg. There was some power in all the muscles of the right arm and right leg. At that examination no contractures or muscular rigidity were observed.

The vision was good. Pupils contracted readily to light; left pupil was smaller than right.

A diagnosis of tumor of the third cervical segment of the cord was made, and operation was suggested as the only means for relief. The following day the case passed into other hands, under the promise of relief without surgical interference. The patient gradually grew worse, and on April 20th Dr. Krauss was called to make an examination, without knowledge of what had gone before or of the diagnosis of the previous examinations.

Careful examinations, both physical and electrical, covering several days, were made, and the diagnosis of spinal cord tumor of the third cervical segment was made, and an operation was urgently advised as the only procedure likely to afford relief. Dr. Roswell Park was asked to operate at this locality, and his report is here appended.

Report of the Operation. (By Roswell Park, M.D.) This was performed April 28, 1902. There was no difference of opinion as to the approximate location of the (supposititious) tumor; the lesion seemed to distinctly involve the third and fourth cervical segments of the cord.

Operation was made difficult by the shortness and stoutness of the neck. The incision extended superficially from the hair line down to the vertebra prominens. Chloroform was the anæsthetic used at first and mostly relied on. When the incision was begun he was breathing about eight times a minute. The position in which he was necessarily placed embarrassed his respiration still more. Before the separation of the muscles from the bone had begun he became cyanosed and ceased breathing. Artificial respiration was promptly resorted to, its necessity threatening to interfere with our antiseptic technique. Subsequent results showed, however, that our precautions were effective.

After thus restoring him the soft structures were rapidly separated on either side from the posterior vertebral surfaces; then with sharp cutting forceps the arches of the third, fourth, and fifth vertebræ were divided, the divided portions lifted and completely removed, and the spinal dura exposed for more than 4 cm. This membrane seemed a little dusky in hue and somewhat distended. With a sharp-pointed small knife I then punctured it at about the middle of the exposed area. Instantly there shot up to a height of at least a foot a tiny jet of cerebro-spinal fluid.

Within a few seconds after the intradural pressure was thus removed his respirations became more full and rapid, and within a few minutes had risen from eight to eighteen a minute.

The dura was then opened to the full length of its exposure. Projecting downward into this opening, partly concealed by the vertebral arch above, was a small tumor, reddish in color, and in appearance much like the choroid plexus, subdural, originating apparently in the pia-arachnoid, in length about 2 cm., its diameter a little longer than that of a common lead-pencil. It was not a difficult matter to detach it from the dura and from the sulcus, where it lay nestled, and then to pull it down from above, and so remove it, apparently, entirely. It was located rather to the right of the middle line, and its most distinct pressure was made upon the posterior columns of the right half of the cord.

The growth was not particularly vascular, and hemorrhage did not uncomfortably complicate the case at any time. As a matter of precaution, however, I applied adrenalin solution, 1 : 1000, on small tampons, and had the satisfaction of seeing the surface dry before closing the dura.

There being no apparent indication for any further intervention, I closed the dura with fine catgut and the balance of the wound with numerous buried sutures of catgut, and finally with silkworm-gut, without drainage. His condition at the conclusion at the operation was much more satisfactory than at its commencement. No plaster-of-Paris or other rigid splint for the head and trunk was used. The dressings were first changed on the third day, then not until the ninth. The wound healed throughout its entire extent by primary union. A microscopic study of the growth, made by Dr. Gaylord, in the State Cancer Laboratory, showed it to be a sarcoma of the round-celled type.

Subsequent History. The condition of the patient was extremely good after the operation, and he made an uninterrupted surgical recovery, which we must credit to the faultless technique of Dr. Park. During the ten weeks since the operation the following changes in his condition have been noted: Motion has returned to all the muscles of the right arm and leg. Sensation of the right side has not returned. Sensation has returned to *the left side*, but the muscles are still without voluntary power, so that at the time of the present writing the patient has the symptoms of Brown-Séquard paralysis—*motion on right side* and some sensation *on the left side.* The reflexes all over the body are still very much exaggerated. The bed-sore is healing under the influence of brewers' yeast. The urine is still passed involuntarily, but the patient is slowly improving. Each week shows increased muscular power and improved sensation. The paroxysms of pain have disappeared, the patient feels comfortable, is buoyant, and hopeful.

From a study of the literature of spinal cord tumors we believe our case to be unique for several reasons: 1. It is the only tumor of the spinal cord affecting the *upper cervical region* which has been so far recorded. 2. It is the only cervical cord tumor which has gone on to an uninterrupted course toward recovery. 3. It was definitely located and quickly removed without sacrifice of spinous processes and laminæ, and the short incision made a remarkably rapid closure. 4. The involvement of the phrenic nerve added an element of danger which was quickly removed during the progress of the operation. 5. From the surgeon's standpoint, it was located in the most inaccessible portion of the spinal cord, by virtue of the cervical curvature of the spinal column offering a concave field for operation instead of a convex.

STUDIES OF OVARIAN EMBRYOMATA, OR SO-CALLED OVARIAN DERMOID CYSTS.

By William Frederick Jelke, M.D.,
INTERNE AT THE LAKESIDE HOSPITAL, CLEVELAND, OHIO.

Everyone who has had the good fortune to study a series of ovarian cysts has found a certain small percentage of them to belong to the so-called dermoid variety. According to Olshausen, about 3½ per cent. of the ovarian cysts are of this kind. The so-called dermoid cysts of the ovary have given rise to so many conflicting views as regards their origin and structure that the literature is full of all kinds of polemics of which they are the subjects. Many of the older theories, themselves, seem to-day to be pathological curiosities. New theories as to their origin have, therefore, been received with a certain amount of reserve. The works of Pfannenstiel,[1] Kroemer,[2] and Wilms,[3] however, seem to have approached more nearly an ultimate solution of the problem than any that have appeared.

It is not the intention of this paper to introduce any new speculations concerning the origin of these tumors, but to describe as accurately as possible three so-called dermoid cysts of the ovary which have come to my hands for pathological diagnosis through the kindness of Dr. D. P. Allen, who removed them. Fortunately these three cysts represent quite distinct and separate features of this kind of new-growth in the ovary, and the study of them has yielded pathological findings similar to those described by Pfannenstiel, Kroemer, and Wilms.

Before beginning the description of these specimens it would seem proper, therefore, to mention briefly some of the conclusions reached by these men, which are exemplified by my pathological findings.

Wilms[3] showed that the so-called ovarian dermoids are to be held distinctively separate from the true dermoid cysts found in the head, neck, thorax, and other parts of the body. He also showed that the "embryome" or "zotte," which is the actively growing, or dynamic, portion of the cyst has representative tissues from each of the three primordial germinal layers, the ectoderm, the mesoderm, and the endoderm; that the order in which these tissues is produced is similar to the physiological process in the formation of the embryo. Accordingly, the skin, hair, teeth, etc.—ectodermal products principally—are the most conspicuous and most highly developed in the "embryome," while the visceral organs are seldom represented; for in the embryo the ectoderm and the cephalic end are differentiated and more highly organized long before the "anlage" of the splanchnic organs and the caudal end are differentiated. Further development to the complete embryo is soon turned aside by the hindrances of pressure and want of space, so that degenerative changes set in and pathological processes supervene which preclude any further development of the embryo as such. By stopping the process of development, thus, at any early stage, when the ectoderm is fairly well developed, the mesoderm less so, and the endoderm represented probably by merely a single layer of cells, it is evident that the last may be overlooked. Hence, it is easy to understand why, in some observations, the absence of representatives from the three primordial layers has been maintained, though a careful microscopic search will show them.

In the normal embryo there is an individual circulatory system very early in the life-history of the organism which is entirely separate from that of the mother, though it receives its soluble nutriment in the plasma through the placenta. In the so-called dermoid of the ovary, on the other hand, there is no placenta, nor is there even any decidual membrane formed in the uterus of the mother, which is one important point that serves to distinctly mark these structures from ovarian or abdominal pregnancies, in which cases an uterine decidua is always formed. The vascular system of the so-called ovarian dermoid is in direct continuity with that of the host without the intervention of a placenta, though, to be sure, new bloodvessels are formed as in all newly developing tissues, and in some cases even a more or less rudimentary bone-marrow is present which may subserve in a small way to the new-formation of blood corpuscles. Such a bone-marrow is found in Specimens 1 and 2.

Wilms then naturally comes to the conclusion that the so-called dermoid of the ovary is not of dermal origin, and is not a true dermoid, but he speaks of the new-growth as a "rudimentary ovarial parasite."

The Germans have referred for a long time to the actively growing portion of these cysts as the "embryome," in order to distinguish them from the true dermoids, which name they reserve for congenital cysts

containing skin, hair, etc., found elsewhere in the body and of different origin. A good translation of this term into English is "embryoma," and I shall use this in referring to the actively growing portion of the cyst in the following descriptions in contradistinction to the whole ovarian cyst, cyst wall, etc.

Pfannenstiel[1] and Kroemer[2] came to the conclusion that the embryoma is of ovulogenous derivation, and that it is not due to a maldevelopment of Pflüger's plugs or cell-nests; nor is it an example of parthenogenesis. They limit parthenogenesis to the physiological process by which a living individual is produced asexually for the purpose of maintaining a species. Pfannenstiel asserts that while the "embryoma" develops from the ovum, the cystic portion of the tumor is derived from the walls of the Graafian follicle.

Dr. J. G. Clark[4] reviews Kroemer's original work, and criticises it very favorably in *Progressive Medicine*, saying in conclusion: "It seems to me that Kroemer has furnished very strong arguments in favor of this theory, and if all his observations can be substantiated there can be no longer any doubt as to its correctness."

Kroemer comes to a full agreement with Wilms, who first offered substantial proof concerning the ovulogenous development of these tumors.

In describing the anatomy of these specimens it would be fruitless, and also beyond the limits of this paper, to go into minute details in respect to the shape assumed by each kind of tissue present, and all the details of its histology, since that would cover the greater part of a treatise on histology, for almost all of the principal tissues of the body are represented in these growths. Also, macroscopically the anatomy of each embryoma differs in greater or less degree from every other one. Therefore, only the more important findings which are characteristic of this kind of new-growth will be described. Also, the macroscopic and microscopic descriptions will not be completely separated, since the aid of the one will be called upon to elucidate or support the findings of the other. Where a conclusion may be drawn from the condition of a tissue found, it will be mentioned immediately, rather than separate these remarks from the picture in question.

Description of Three Cysts and Their Contents.

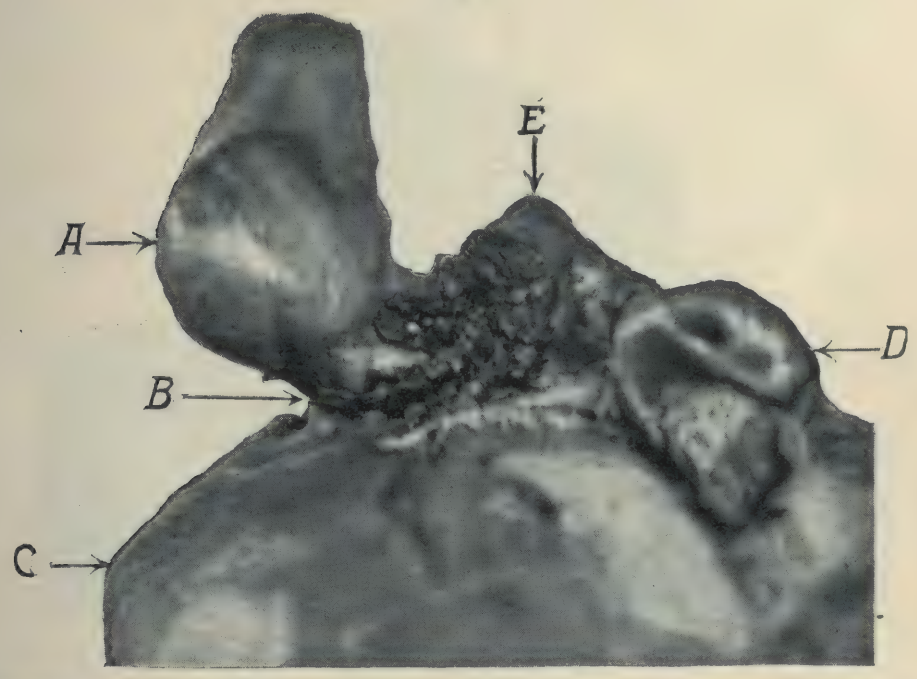
Specimen 1 (Fig. 1) was removed from Mrs. H. A., aged forty-eight years, nationality Russian. She had had eleven living children and two miscarriages. Family and personal histories unimportant, with the exception that sixteen years ago the patient was told she had a tumor in the pelvis about the size of a lemon. This increased gradually in size until some years later, when she began to feel the tumor herself

above the brim of the pelvis. The tumor caused no pain, nor did it interfere with repeated pregnancies.

The tumor was removed July 28, 1902, by Dr. Allen, on account of pressure and urinary disturbances it was causing.

Macroscopically the tumor is found to be a cyst of the right ovary, measuring 13 cm. in diameter and of $1\frac{1}{2}$ litres content. The exterior of the cyst is of a dull yellowish white, in places shading into a bluish color. The surface is for the most part smooth, only here and there roughened by a few small tabs of fibrous adhesions. The right ovary and tube are adherent to the cyst, and also a portion of the fimbriated end of the left tube is adherent. Dark-blue bloodvessels can be seen radiating throughout the surface; they do not appear to be deeply

FIG. 1.



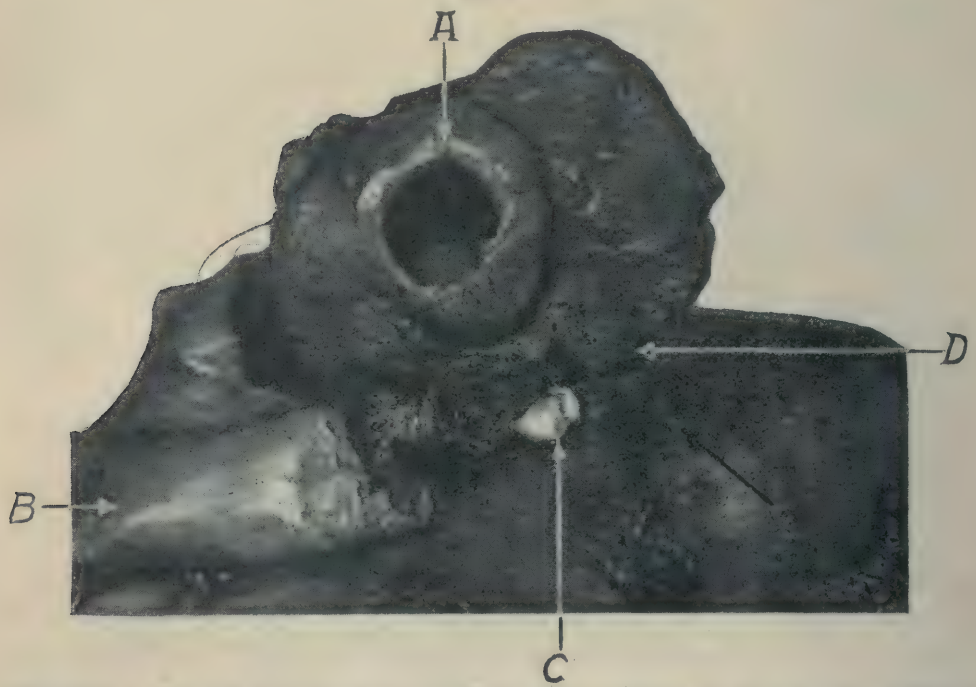
Specimen 1. Exterior of a portion of the cyst and adnexa. *A*. Cystic ovary. *B*. Bridge of tissue joining the cyst to a pole of ovary. *C*. External surface of cyst showing a few dark shadows of bloodvessels. *D*. Fallopian tube near uterine end. *E*. Fallopian tube near fimbria. (Natural size.)

situated in the cyst wall, but rather superficially. No inflammatory process, either past or present, can be made out in the ovary or tube. The former has a smooth exterior, except where attached by one pole to the large cyst; the latter is adherent only in part of its course, and its fimbriated end is free and patent; the lumen contains no pus. The wall of the cyst is very tough and leathery. In one place there is a small, thin area through which a hard body can be felt in the interior.

The lumen of the cyst is found to be unilocular, and to be filled with a thick, brown, pasty mass that has a faint aromatic odor. This mass

has a very greasy consistency when rubbed between the fingers. When exposed to the air at room temperature it rapidly solidifies and looks like beef fat or suet. Under the microscope it is composed of round balls of highly refractile, white-looking material. These balls or droplets dissolve readily in ether and warm alcohol, but separate out in cold alcohol or water. No crystals of cholesterin or other crystalline bodies are present. No leucocytes or other cells are seen, and no bacteria are found in the cover-slip preparations. Cultures tried on the usual media proved to be sterile. In the midst of this pultaceous mass is a ball of tangled, coarse, blonde hair. Almost all of the hair is found loose in the cavity, and is not attached to the inner surface of the cyst. The inside lining of the cyst does not resemble skin, nor does it

FIG. 2.



Specimen 1. Showing the embryoma everted through an opening in the cyst wall. *A*. Lip of ostium to the sac-like cavity in the embryoma. *B*. Cyst-wall, opened to show embryoma. *C*. Bicuspid tooth. *D*. Portion of the bone underlying soft parts. The black arrow indicates the direction of the transverse section surface shown in Fig. 4. (Natural size.)

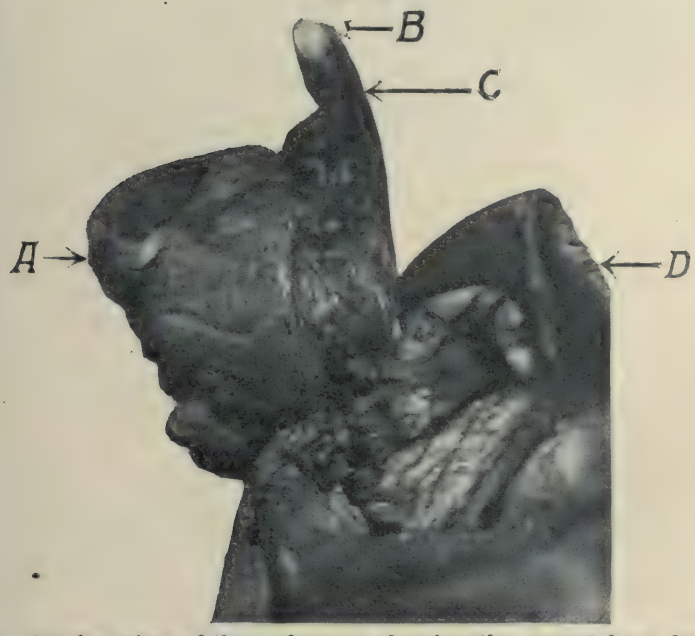
appear capable of bearing hair. Therefore, this large amount of hair must have been produced from the single point on the inside of the cyst wall from which the embryoma or "zotte" protrudes. Also, the fatty, sebaceous-like material derives its origin from the same source.

Projecting into the cyst lumen from its inner surface at a point 10½ cm. from the connection of the cyst wall externally with the ovary is a mass of bone and soft tissue. (Fig. 2.) This mass forms the "embryoma," and measures in this case 4½ x 3½ x 2 cm. A well-formed bicuspid tooth is seen projecting conspicuously from an exposed portion

of the bone. The bony portion of this structure is situated next to the cyst wall and underlies and supports the soft parts which cover the aspect turned toward the cyst lumen.

The shape of the bone is curved, the convex surface being turned toward the cyst wall. (Fig. 3.) This surface is completely flattened and smoothed. At the apex or the most prominent portion of the bone is situated a large bicuspid tooth. Now, at the first glance one is struck by the apparent resemblance of this portion of the bone to the lower maxilla in the adult. Due to its curved shape and the insertion of the tooth at the end, the total effect is that of an atrophied mandible in an old person who still possesses a single front incisor tooth, with the molar and bicuspid teeth lacking and an atrophied thin jawbone remaining.

FIG. 3.



Specimen 1. Another view of the embryoma showing the curved bone having the same curvature as the cyst wall. *A*. Embryoma, upper surface near the mouth of the cavity. *B*. Bicuspid tooth at apex of the bone. *C*. Convex surface of curved bone. *D*. Cyst wall. (About natural size.)

It is not the intention here to draw a close morphological comparison between this specimen and the senile lower jaw, but simply to show how far the imagination of the describers of many such specimens in the past has led them astray.

Some of the forces which produced the shape of this bone are made evident by noting its relation to the cyst wall. The curvature of the bone is that of a segment of a circle exactly coinciding with the inner surface of the cyst wall. The side of the bone next to the wall of the cyst is perfectly smooth and polished, and fits into a depression of the wall, which has likewise a smooth bottom. This depression in the wall has the exact outline of the bone, and serves as a matrix into which it is

set. There is no organic union between the bone and the cyst wall over this area, so that it is evident that the bone did not originate from the cyst wall, but is a lateral growth from the embryoma. It was through this thinnest portion of the wall that a solid body could be felt from the outside. When held up to the light one could almost see through this portion of the wall, it was so thin and translucent. In short, this thinnest area was produced by local atrophy, due to pressure on part of the bone. The surface of the bone, on the other hand, was made smooth and moulded so as to conform with the curvature of the cyst. The side of the bone toward the cyst lumen was free to develop, and hence had a more irregular outline, and at one point a tooth was produced. This tooth, however, is a bicuspid tooth, though it is in a position usually occupied by an incisor tooth, if this were, in reality, an attempt to form the lower maxilla. The side of the bone turned toward the cyst cavity was covered with a thin membrane, probably periosteum, while that facing the cyst wall was bare bone. Hence, the shape assumed by this bone was not due to a mimicry on the part of the embryoma to produce an organ similar to that found in the adult body, but it was moulded by external forces, to which it finally succumbed and resulted in a good example of pressure atrophy.

The soft parts are covered with a very coarse, hairy skin. The mouths of the large sebaceous glands are distinctly visible to the naked eye. The hair, however, has almost entirely fallen off. Directly above the point where the tooth appears in Fig. 2 is a globular, sac-like body, with a large round, smooth mouth. The wall of this structure is over 2 mm. thick, and is covered on the outside with fairly normal looking skin, which contains hair follicles, sebaceous and sweat glands. At the margin or lip of the ostium of this pouch a direct transition to smooth squamous epithelium void of hair or sebaceous glands takes place, and reminds one of the transition in the epithelium of the normal human lip. This same mucous epithelium lines the entire inner surface of this small cavity, which measures $2\frac{1}{2}$ x 2 cm. A cross-section of it may be seen in Fig. 4.

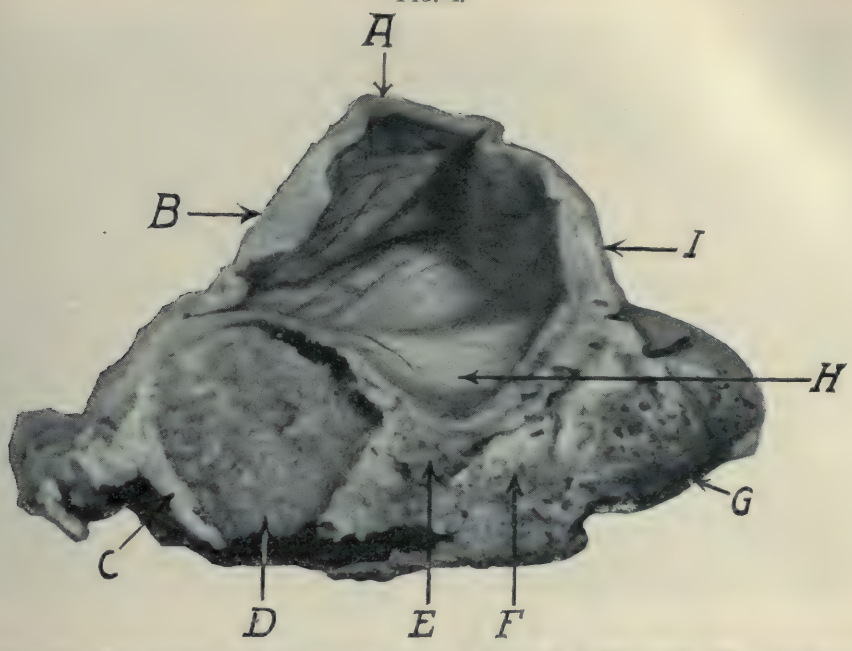
The wall of this cavity is constructed of fibrous and fatty tissues which surround the sebaceous glands that open toward the outer or skin surface, while the little cushion of fat and loosely held together connective tissue bulges toward the cavity on the inside.

The complete microscopic study of this specimen was greatly embarrassed by the profound hyaline degeneration that had taken place in the soft tissues, so that only good microscopic pictures could be obtained of the firmer tissues, bone, cartilage, and dentine. The reason for this hyaline transformation will be considered below.

A distinct zone of well-developed hyaline cartilage was found between the bone on the lower side and the soft structure above. Between the

cartilage and soft tissue a narrow strip of fibrous tissue could be seen. The bone presented near the centre a well-formed medullary cavity

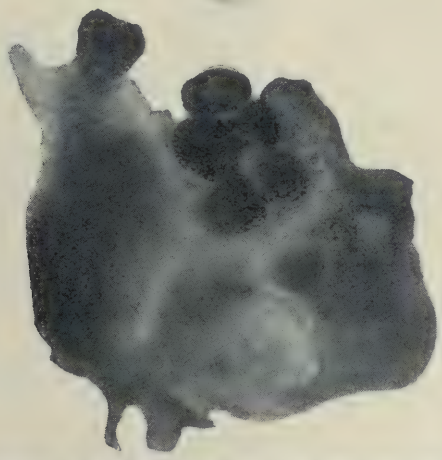
FIG. 4.



Specimen 1. Cross-section of embryoma taken in a plane indicated by the black arrow in Fig. 2. *A*. Lip of ostium. *B*. Skin and hair-bearing surface, also showing a fat cushion bulging toward the interior of the cavity. *C*. Solid laminated bone. *D*. Bone-marrow. *E*. Site where corpora amylacea were found. *F*. Site of a large mass of cartilage. *G*. Cancellous bone. *H*. Internal surface of sac-like cavity lined with mucous epithelium. *I*. Skin surface of embryoma furnished with sebaceous glands and hair follicles. (Enlarged about twice natural size.)

filled with fat, red blood cells, and leucocytes of various kinds. This cavity was crossed by a few trabeculæ of cancellous bone.

FIG. 5.

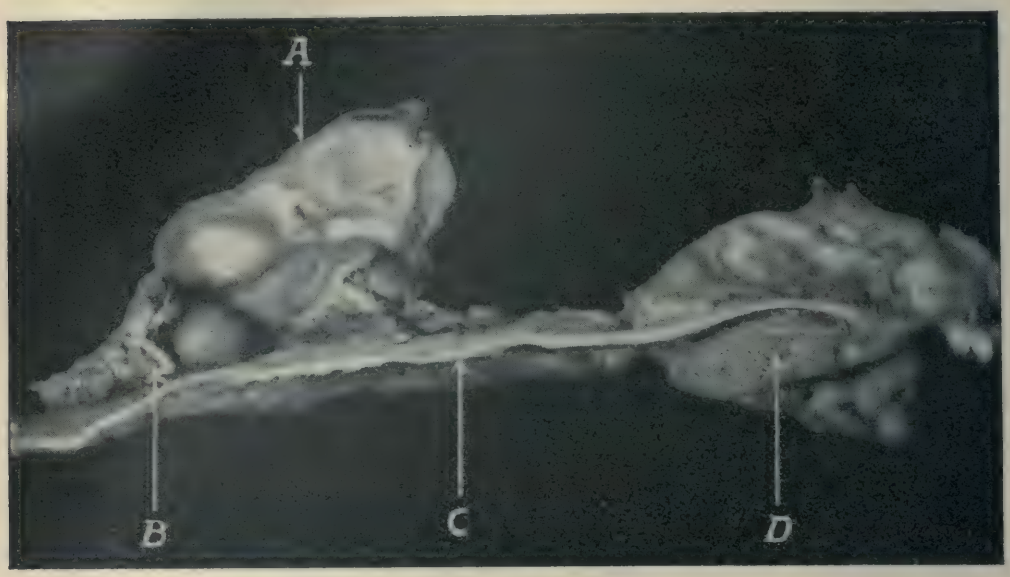


Specimen 1. X-ray photograph of embryoma showing five more teeth besides the one exposed bicuspid tooth at the top, which is the only one seen in the other photographs. (Natural size.)

At the point indicated in Fig. 4, *E*, a large group of corpora amylacea was found. As many as 175 were counted in one field

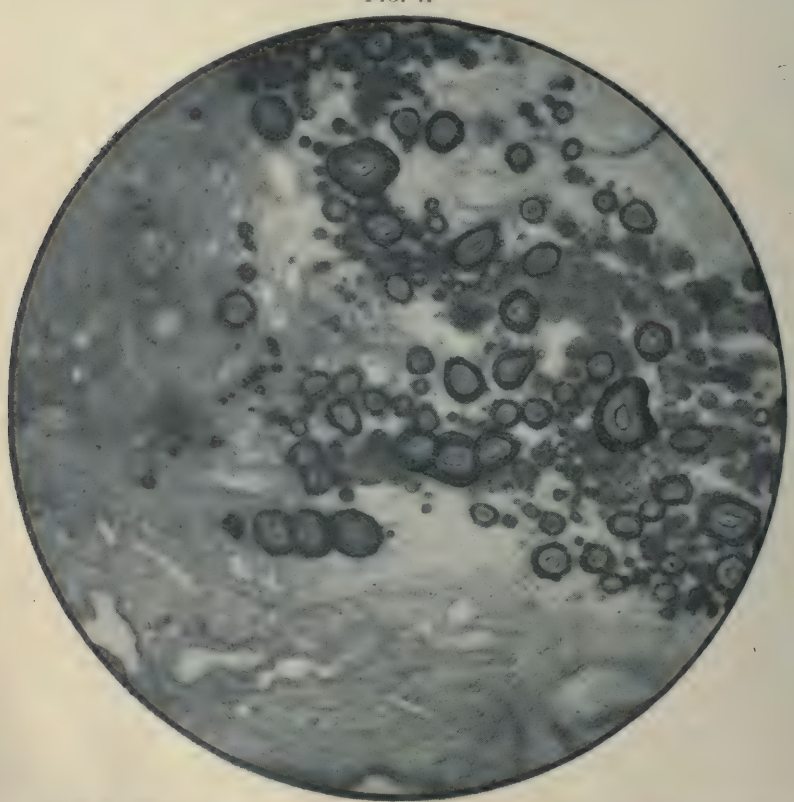
of the microscope with low-power objective. Some of the sections were stained in various ways so as to make sure of their composition.

FIG. 6.



Specimen 1. Showing the cyst wall intervening between and serving to join the ovary with the embryoma. *A*. Cystic ovary. *B*. Fimbriated end of Fallopian tube. *C*. Thin edge of cyst wall joining the embryoma to the ovary. The ovary extends on the external surface of the cyst wall, while the embryoma is situated on the inner surface and bulges toward the cyst lumen. *D*. Embryoma. (Reduced in size.)

FIG. 7.

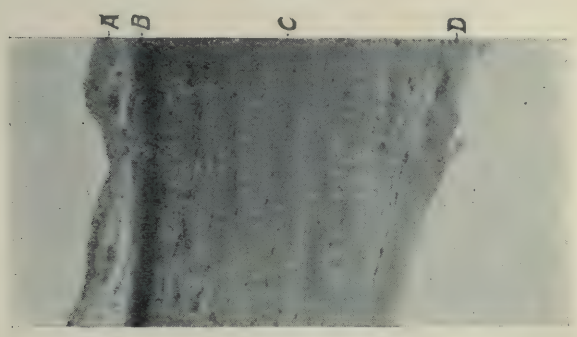


Specimen 1. Corpora amylacea found at point indicated in Fig. 4, *E*. (Magnified about 80 times.)

They reacted typically to the iodine and sulphuric acid test, first made known by Virchow in 1854. Also, typical reactions were obtained with methyl violet and methyl green. That they also contained some calcareous material was evident from the avidity with which they absorbed hæmatoxylin. This fact suggested the possibility of their relationship to the psammoma bodies of the central nervous tissues, though in this case they were found in a degenerated glandular tissue. Morphologically, the usual hyaline-like layers were seen to be deposited around a bright, central, highly refractile nucleus, the whole body having a concentrically laminated structure.

These bodies were described first by Morgagni, in 1723, and have since, from time to time, given rise to much discussion concerning their nature and origin. Exhaustive studies on this subject may be found in the works of H. Stilling[5] and Ferdinand Siegert.[6] The general con-

FIG. 8.



Specimen 1. Section through cyst wall near the ovarian attachment. *A*. External surface of cyst wall, with remains of ovarian tissue. *B*. The line marking theca externa. *C*. Theca interna increased greatly in thickness by fibrous tissue, which is poor in bloodvessels. *D*. Layer of cells similar to corpus luteum cells.

sensus of opinion is that they are found in senile tissues more abundantly than elsewhere, as in the central nervous system, lungs, and prostates of old men, and that the tissues in which they are found have undergone atrophic degenerations.

The most interesting feature of this specimen is the fact that the embryoma is situated $10\frac{1}{2}$ cm. from the ovary which gave rise to it, as was mentioned above. The only connection of this body, which is considerably larger than the ovary, with the pole of the ovary which gave rise to it is by means of the thin cyst wall. This suggested the question: "From whence did the embryoma receive its blood supply and nutriment during the last sixteen years of its existence?" For we were assured by the patient that the cyst was the size of a lemon sixteen years ago. Thereupon, serial sections were cut out of the short pedicle between the ovary and the cyst, and also many sections were taken from the cyst wall lying between the ovary and the embryoma,

with the view of searching for the blood supply. It was found that there were very few bloodvessels present in the pedicle, and still less in the cyst wall, scarcely sufficient to supply the latter, much less the embryoma. The structure of the cyst wall was found to correspond with that of the ordinary corpus luteum cyst and to show two distinct fibrous layers of the theca externa and theca interna, the latter being very poor in bloodvessels, and in some places showing marked hyaline degeneration.

The interior of the cyst was lined with several layers of large cells irregularly packed together, containing large pale nuclei that resembled the corpus luteum cells lining a corpus luteum cyst. Hence, it became evident that the embryoma had developed in a Graafian follicle at one pole of the ovary. That the cyst wall had not taken part in the production of the embryoma, but it had remained a passive factor in the process, and that the lumen of the cyst had merely taken the place of a receptacle into which the loose hair, squamous cells, débris, and excretions of the sebaceous glands of the embryoma had discharged themselves. Thus, the constant increase in the contents of the cyst had gradually distended its walls and increased the size of the cyst; by increasing the size and periphery of the cyst the embryoma had been gradually carried away from the pole of the ovary from which it originated. The constant pressure from within had caused tension on the cyst wall, with a gradual occlusion of the bloodvessels supplying the embryoma.

This cutting off of the blood supply would easily explain the general hyaline degeneration that had taken place in the embryoma.

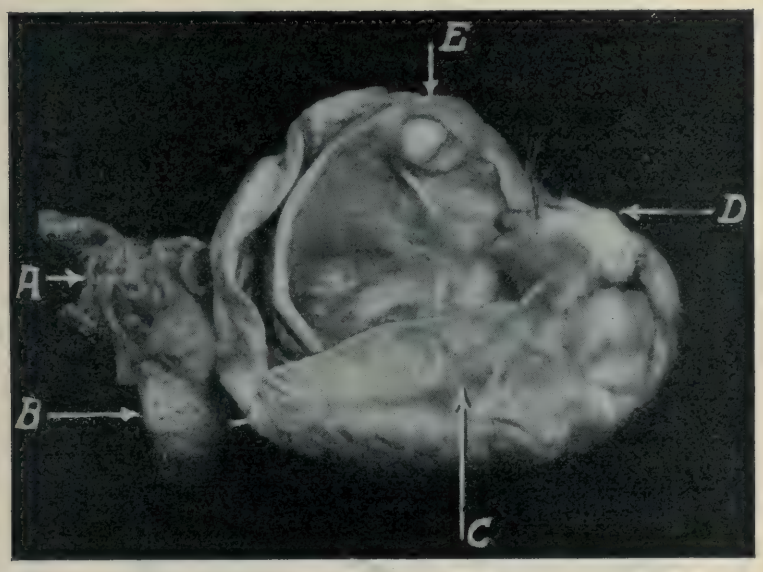
The X-ray photograph shows five more teeth besides the one large exposed bicuspid tooth. These teeth were inserted in the cancellous bone underlying the soft tissues, and had not yet cut through to the surface, and their presence was not discovered until the shadow was obtained on the X-ray plate. Sections were studied from the ovary which was removed with the cyst, and it was found to contain several small follicular cysts; two of them measuring over 1 cm. in diameter. There are no normal follicles to be seen in the cortical portion, and the stroma shows a general senile atrophy.

Specimen 2 was removed from Mrs. B. S., aged twenty-two years; nationality Russian. Family and personal histories unimportant until thirteen months ago, when she was in confinement. Since then she has complained of pain in the lower portion of the pelvis, which has greatly increased during the last six weeks. She was operated on May 23, 1902, by Dr. D. P. Allen, who removed a tubo-ovarian mass from the left side, which was greatly inflamed. This mass on fresh section was composed of clotted blood and a soft spongy tissue, which, on further microscopic study, proved to be an early tubal pregnancy. From the right side was removed the specimen here to be described.

The Fallopian tube on the right side is found to be normal. The ovary on this side is normal in size, measuring 4 x 4 x 3 cm., but is soft and studded with small cysts about the size of a pea. These were found later to be the maturing Graafian follicles. The surface of the ovary is white and glistening, and shows no signs of inflammatory reaction; there are no adhesions on this side. Upon section of the ovary it is found to be filled with a yellow, thick, semifluid material, which is quite greasy. Cultures grown in the usual media remained sterile.

After carefully removing this semisolid mass, in which were found a few loose hairs, a small portion of bone was exposed, in which was inserted a bicuspid tooth. Near one end of this plate of bone a soft,

FIG. 9.

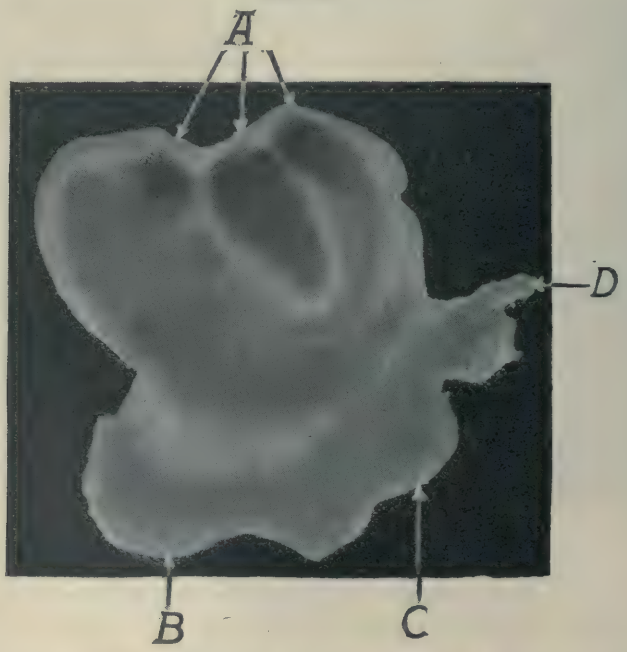


Specimen 2. Shows the ovary opened by a longitudinal incision. *A*. Fimbriated end of Fallopian tube. *B*. Fallopian tube. *C*. External surface of ovary and wall of cyst, showing small cystic follicles on uneven surface. *D*. Embryoma, with soft tissue and tuft of hair. *E*. Bony portion of embryo and single bicuspid tooth.

irregular spongy body was found covered with skin, from which protruded a small tuft of hair. The bony portion seemed to arise from one side of the cyst only, and occupied about one-third of the inner surface of the cyst; the latter was drawn over the remainder of the embryoma as a sac-like covering. In other words, this is the same condition as was found in Specimen 1, only in this case the cyst is much smaller in proportion to the embryoma. Here the embryoma fills almost the entire cyst lumen, and the greater portion of the embryoma, macroscopically, is seen to be composed of bone, while the skin and hair-bearing surface is reduced to a small area of about 1 x 1½ cm. In the former case, Specimen 1, the skin and hair-bearing surface was considerable, covering the greater portion of the embryoma, and, conse-

quently, the cast-off hair and excretions from the skin formed the largest and most conspicuous portion of the cystic contents. Here, then, is good evidence that the cyst lumen serves chiefly as a receptacle for the excretions from the dermal surface of the embryoma, and that the size and distention of the cyst are in direct ratio to the amount of waste products shed from the embryoma. The shape of the bone was fairly regular and disk-shaped, with two small undulating prominences, which, on comparing with the X-ray shadow, were seen to be the site of two teeth not yet cut through the surface. This was substantiated later by transverse microtome sections. This bony portion of the embryoma was covered with a thin, firm, smooth tissue that had a moist, sticky surface entirely void of hair and not resembling normal skin, but looked more like mucous membrane.

FIG. 10.



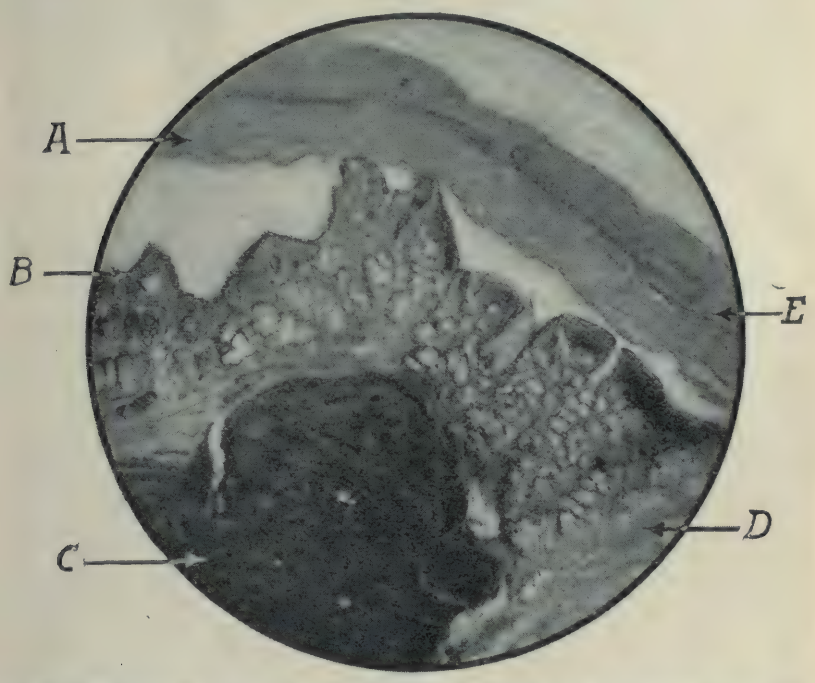
Specimen 2. X-ray photograph showing two more teeth in addition to the single bicuspid tooth in Fig. 9. *A*. The three teeth. *B* and *C*. Fallopian tube. *D*. Fimbriated end of Fallopian tube.

After this superficial investigation, the longitudinal incision through the cyst wall was tightly sutured, so as to restore as nearly as possible the relation of the embryoma to the cyst. The whole mass was then decalcified, and sections were cut.

Microtome sections were cut transversely to the long axis of the ovary through the cyst wall, soft parts, bone, and teeth. The cyst wall is seen to contain ovarian stroma in all portions, so that the embryoma, which is centrally located in the ovary and arises from the thickest part of the cyst wall, must have arisen in a Graafian follicle near the medullary portion of the ovary, and not in the cortical portion.

The soft parts are covered with a true skin at the end of the embryoma, from which the tuft of hair may be seen growing. This skin is remarkable in the great amount of comedone formation present. That is, the ducts of the sebaceous glands have become stopped, and minute retention cysts have formed, which have subsequently broken through to the surface, causing the skin to have a very rough, uneven, honey-combed appearance. The epidermis is normal, having a well-defined corneous layer, and shows the transition from squamous to polyhedral cells in the deeper layers. The corium is well developed and contains fibrous and fatty tissue, which is penetrated by the hair shafts springing from

FIG. 11.



Specimen 2. Microscopic section through a portion of the cyst wall and embryoma. *A*. Cyst wall containing ovarian tissue. *B*. Epidermis of embryoma thrown into an irregular, broken surface by the comedone formation in the sebaceous glands. *C*. Firm lamellated bone showing Haversian canals. *D*. Corium of skin containing large masses of sebaceous glands. *E*. Cyst wall containing a long flattened corpus albicans in the ovarian tissue. (Magnified about 40 times.)

normal hair papillæ. The size and number of the sebaceous glands are far greater than normal, and hence, the condition may be looked on as an hypertrophy and proliferation.

Around the bases of these glands is seen the fibrous tissue of the corium held together in loose bundles; in other places fat cells are more predominant.

In the corium are seen masses of tubular glands lined with a single layer of low cuboidal epithelium, with large round deeply staining basal nuclei. These cells rest on a firm homogeneous highly refractile narrow band of tissue that may be considered the membrana propria, which

separates the gland tubules from the connective tissue of the stroma and from each other. These glands, without doubt, bear a strong resemblance to sweat glands; but, due to the great number of sebaceous glands above them, it is difficult to find ducts long enough to penetrate in one continuous line to the surface of the epidermis in one section, though cross and oblique sections of such ducts are frequently seen.

The soft parts at the other end of the specimen show a rather complex set of foldings and reduplications. Here the epidermis is quite

FIG. 12.



Specimen 3. Interior surface of cyst wall, showing the flattened embryoma. The tuft of hair is seen springing from the skin surface, which is dotted over with large mouths of sebaceous glands. (A trifle enlarged.)

thin, though of the squamous variety; it contains no papillæ, and is only four or six cells deep in some places. No glands of any description underlie this epithelium. There is a marked change in the surface, which rises up to form regular papillæ or villi, covered with low columnar epithelium, with round vesicular nuclei placed at the base of the cell. Where cross-sections of these villi are met they are seen to be uniformly round or oval in contour; and the epithelial cells rest on a fine basement membrane. The body or core of the villus consists of fibrous connective tissue regularly placed around small vessels. A few leucocytes and red blood corpuscles are seen in the meshes of the con-

nective tissue. These structures then resemble closely the villi of the small intestine. On following this undulating surface into some of the other folds, a transition from squamous epithelium to high columnar ciliated epithelium is seen. These columnar cells have large, oval basal nuclei. Between them are placed many interstitial cells, and the whole mucosa is bounded by a distinct limiting membrane. This tissue is seen to contain many small round deeply stained leucocytes, and in

FIG. 13.



Specimen 3. Microscopic photograph showing representatives from the three primitive layers. *A*. Epidermis with the mouth of an immense sebaceous gland. *B*. Rudimentary thyroid gland containing colloid material in the acini. *C*. Large mass of lymphoid tissue. D. Bloodvessels in corium surrounded by fibrous and fatty tissue.

some fields of the microscope they are found massed together into structures resembling solitary follicles.

The more highly differentiated glandular structures found in the normal intestinal wall, like the glands of Brunner and the follicles of Lieberkühn, are absent.

The bone in this specimen is macroscopically irregular and of a nondescript form, but microscopically it contains all the structures of

normal bone. A large portion of it has a cancellous structure, and the spaces are filled with red and yellow marrow. The teeth have all the structures found in normal teeth. The dentine is laid down in perfectly parallel dentinal tubules, and the pulp cavity is seen to contain normal bloodvessels and fibrous tissue.

The sections through the remainder of the ovary lying outside of the cyst wall show numerous Graafian follicles in various stages of maturity, and some of the follicles are so large as to become small cysts. These large follicles are situated in the cortex of the organ, but there is still considerable dense ovarian stroma separating them from the surface. It is rare to see so many apparently mature follicles and others rapidly approaching maturity in a single section as the sections from this specimen show.

Specimen 3 was removed from Miss I. W., aged twenty-five years; teacher; nationality American. Family and personal histories unimportant. During the last two years she has had some uterine trouble and has complained of increased frequency in menstrual periods, for which she received local treatment. On September 4, 1902, Dr. D. P. Allen removed the specimen, now to be described, from the left ovary.

This consists of a cyst measuring 12 x 9 x 7½ cm., or about the size of a large orange, weighs 460 grammes, and is ovoid in shape, with a fairly regular outline. The exterior has a glistening, pale, yellowish-white color. No adhesions are present. The tube is firmly stretched over the cyst in the middle of its course, but both ends are free and patent. In short, there are no evidences of inflammation past or present.

The exterior of the cyst is of a light-yellow color, in places shading to a dark blue or purple. Immediately after removal the cyst appeared to contain fluid, and fluctuation of its contents was noted; by the time the operation was over, however, it had cooled down to room temperature, and was found to be much firmer than when removed; fluctuation could not be obtained, but the contents could be kneaded like putty. It was then evident, before the cyst was opened, that it belonged to the variety that we are now considering.

On opening the cyst it was found to be filled with a light-yellow, greasy material which resembled butter. This was thoroughly mixed with a tangled mass of dark-brown hair. Cultures grown on the usual media remained sterile.

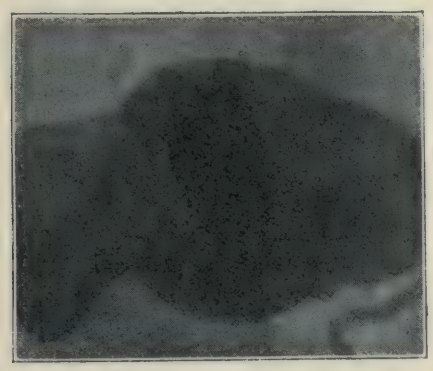
The oleaginous portion of the cystic contents was easily soluble in ether and warm alcohol, but not in cold alcohol or water. When examined under the microscope it was seen to be made up of small, highly refractile balls or droplets. A portion of it was treated with a dilute solution of warm potassium hydroxide, and it was saponified. No cholesterin or other crystals were found, nor were there any leu-

cocytes to be seen, but merely the desquamated epidermal cells and débris.

In this case the cyst was bilocular, that is, there were two large loculi; one, however, about twice the size of the other, contained the hair, and in this one the embryoma was found. The smaller cyst contained a thick, viscous fluid, partly mixed with the oily substance derived from the other cyst, for a small perforation was found in the septum between them.

The embryoma was found quite flattened against one side of the cyst, and appeared directly continuous with the ovary, which was flattened and stretched on the outside of the cyst. The shape of the embryoma was more irregular in this case than in either of the others, but, in general, it assumed that of a bar or bridge of tissue stretching across a segment of the cyst and having irregular expansions on the cyst wall at either end.

FIG. 14.



Specimen 3. X-ray photograph showing the small almond-shaped piece of bone with one tooth lying in the centre of the embryoma, which shows in lighter shadow.

The side of the embryoma turned toward the cyst lumen had a large superficial expansion, and was covered with hair and the mouths of large sebaceous glands. The lower or under side of the tumor was covered with a smooth, almost velvety epithelium, possessing no hair or visible gland orifices.

This embryoma is the smallest of the three, measuring 5 cm. long by 2.2 cm. wide, but has relatively the largest skin and hair-producing surface. The size of the cyst, though not actually so large as Specimen No. 1, was relatively to the embryoma very much greater. Here, then, was a large cyst with a relatively large skin and hair surface on the embryoma. In other words, this substantiated the fact above noted, that the cyst serves simply as a receptacle for the excretions of the embryoma, and where a large cyst is present a correspondingly large surface for the production of the cystic contents must naturally be expected. In Specimen No. 2 the skin and hair-producing surface was

seen to be quite small; in that case the cyst did not go beyond the limits of a normal sized ovary. Only one hard, firm nodule, about the size of an almond, could be felt in the body of the embryoma. This was shown by the X-ray shadow to be composed of a small piece of bone and one tooth. (Fig. 14). No teeth were visible on the surface of the embryoma. The line of demarcation between the skin covering the embryoma and the interior surface of the cyst wall was very distinct.

In the macroscopic description it was noted that the embryoma was attached at either end to the cyst wall, but was free in the cyst lumen near its central portion. One of these ends was seen to arise opposite the point where the ovary was attached on the other side of the cyst wall; for the sake of convenience in the description this will be designated the proximal end of the embryoma, being nearest the ovary, while the other end will be referred to as the distal end. Microtome sections were begun at the proximal end and cut transversely to the long axis of the embryoma.

The first set of sections were carried through the ovary, cyst wall, and proximal end of the embryoma. The layer of ovarian tissue is seen to be very much flattened and thinned with the cells of the stroma densely packed together.

Next to this is the cyst wall, composed of dense strands of fibrous tissue laid in parallel bundles. The cyst wall in this case is the one most richly furnished with bloodvessels of the three specimens. A definite arrangement of the layers into a theca interna and theca externa can be made out as in the other two cysts.

The proximal end of the dermoid is composed chiefly of loosely packed connective tissue, which is well supplied with large bloodvessels. Some of the intervascular connective tissue is seen to be undergoing an apparent myxomatous change. In these areas the cells are seen to be greatly swollen, the cytoplasm being pulled out into long, thin processes, which take a very faint eosin stain. Some of the cells appear purple on account of the indifferent way in which they take both the hæmatoxylin and eosin. The nuclei still retain their staining properties, though they are large, pale, and vesicular.

In some places where the change is most extensive only the nuclei can be seen, the cytoplasm and intercellular substance no longer being differentiated by the stains. Such areas look very much like soft, medullary, sarcomatous tissue. The altered tissue does not appear malignant, however, and such changes in ovarian tissue and ovarian tumors are not uncommon. There are numerous small, round, lymphoid cells throughout this portion of the preparation, and here and there they may be seen massed into large groups that appear like lymph nodes. The upper and lower surfaces of the embryoma near the proximal end are covered with squamous epithelium; that on the upper surface is

thicker than that on the lower, though no hair follicles or glandular structures are to be seen in this portion of the specimen.

The next block of sections was taken from the middle portion of the embryoma, and involved the soft parts and the bone discovered by the X-ray shadow. The upper surface or side of the embryoma turned toward the cyst lumen in these sections is that portion which is seen to be so richly supplied with hair. Here the epidermis is of normal thickness, but the corium is very much increased in depth on account of the large number of hair shafts and the great increase of sebaceous glands that dip down into it. A definite pigment layer is easily made out in the epidermis in this case. Below the sebaceous glands a narrow band of non-striated muscle is seen weaving its way in a wavy outline across the specimen near the fundi of the sebaceous glands. Bundles of nerve tissues are also easily made out. These bundles appear like the trunks of normal peripheral nerves, composed of axis-cylinder and myelin sheath. These bundles can be traced into the next set of sections taken from the distal end of the embryoma, in which ganglion cells are found.

Islands of cartilage of various sizes, with perfectly normal cells, are present. Some of these islands are long and narrow, and it is evident that an attempt has been made to form a chain of strips or islands of cartilage, but a complete ring has not been formed, such as occurs in a normal trachea. As the lower side of the section is approached (corresponding to the lower side of the embryoma), the connective tissue is less dense, and here and there is replaced by islands of fat. Large masses of lymphoid cells are also met. Finally the lower border of the section is seen to be covered with a single layer of ciliated columnar epithelium. The small section of bone in this specimen is quite dense, and no cancellous tissue is present. The arrangement of the lamellæ and Haversian canals is normal.

The third set of sections, involving the cyst wall and the distal end of the embryoma, shows the same great variety of tissues as the preceding sections. In addition, a rudimentary, mucous, salivary gland, showing all the details of the normal structure, including acini and tubules, is present. These tubules are quite distinct, and the acini are separated by a considerable amount of fibrous tissue; the definite racemose character of the glands is well marked.

Tissue resembling normal thyroid gland, with well-marked spaces filled with colloid material, is present. One of the most interesting histological details of the sections from this part of the embryoma is the well-developed ganglion containing large nerve cells, such as are seen in the dorsal root ganglia of the spinal sensory nerves.

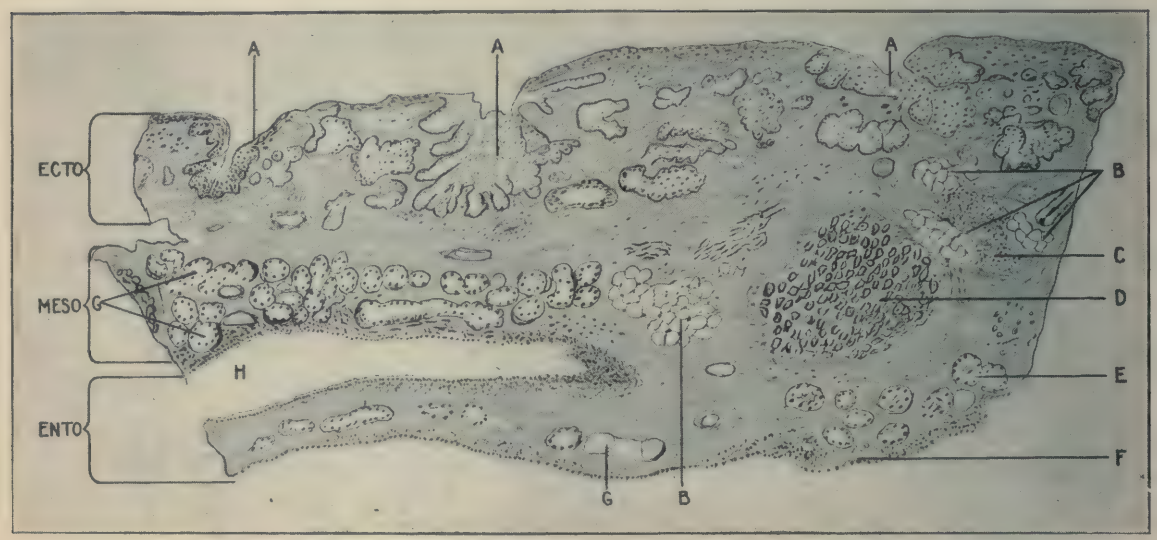
Space would not permit, here, to go into all of the histological details of the representatives of the various glands, tissues, and structures occurring in the upper portions of the respiratory and alimentary tracts

found in this specimen. Such would be merely a repetition of well-known histological pictures.

Taking the general relation of these structures to one another into consideration, however, it is interesting to see that they had a fairly definite order, beginning with the ectodermal derivatives on the superior surface (the skin, hair, and sebaceous glands), followed by the mesodermal structures (connective tissues, bone, fibrous tissue, cartilage, etc.) near the centre of the embryoma, and finally furnished with the derivatives of the endoderm (the ciliated columnar epithelium, thyroid gland, and a structure similar to the intestinal canal) near the lower surface of the embryoma. (Fig. 15.)

The most extensively developed layer is the ectodermal, the least differentiated the endodermal.

FIG. 15.



Specimen 3. This is a photograph of a drawing made with a camera lucida of a section showing the representative tissues derived from three primordial layers. The outlines are perfectly preserved, though the nuclei were put in free-hand and show up too large in proportion to the magnification. *A*. Large sebaceous glands. *B*. Fat. *C*. Lymphoid tissue. *D*. Cartilage. *E*. Thyroid tissue. *F*. Ciliated columnar epithelium. *G*. Salivary gland tissue. *H*. Cavity lined with ciliated columnar epithelium. *Ecto*, *Meso*, and *Ento* represent in a general way the three zones of the embryoma in which representatives from the three primordial germinal layers may be found. (Magnified about 12 times.)

The cells representing these tissues are in every case as perfect of their kind as those found in normal adult organs; but, on the other hand, the organs themselves have in no case reached a normal and full completion. In other words, the picture produced is that of normal adult cells placed in the positions of embryoidal beginnings of organs. The necessary foldings and mechanical action in the migration of the various cells has not taken place. To use a military simile, one might aptly describe the position of these adult cells as one in which no mobilization had

occurred, or in which they had not been mustered into their proper ranks.

The bizarre form assumed by the tissues of this and other specimens would then be explained as in Specimen No. 1, namely, that extraneous forces had so hemmed the development along normal lines as to sooner or later arrest the growth. Also, the fact must not be forgotten that here a large portion of the embryoma is held stationary against the cyst wall, so that the normal foldings and invaginations of the various tissues cannot take place as in the normal embryo, which is practically swung free in space in the amniotic fluid.

SUMMARY. 1. It has been shown in these specimens just described that, though each has an anatomy peculiar to itself, still there is much in common among them, and also that they are similar to the cases recorded by Pfannenstiel, Kroemer, Wilms, and others.

2. Structures derived from the three embryonal primordial layers were found in each of them, with the exception of the first, and here the microscopic search for the endoderm was prevented by the great degeneration of the tissues, so that only the coarser structures could be made out.

3. The extent of the development along different lines varied greatly in each case, though all of them were turned to pathological growth comparatively early when compared with the normal embryo.

4. The structure of the cyst wall was seen to be similar to other cysts derived from Graafian follicles.

5. The size of the cyst was independent of the size of the embryoma within certain limits, but the size of the cyst seemed to vary in direct proportion to the amount of waste matter excreted by the embryoma.

6. The remains of the ovary from which these specimens developed, as well as the organ on the opposite side, were found to be either cystic or to have an abnormally large number of follicles approaching maturity.

7. In none of the specimens were any fœtal inclusions, fœtal remains, or congenital malformations found, and that the rest of the genitalia of the hosts was normal with the exception of the cystitis in Case I., and the tubal pregnancy in Case II. So that the congenital formation of these tumors appears extremely doubtful.

It seems necessary to mention, however, for sake of completeness, that such congenital origin for these new-growths has been maintained by Bandler[7] since the works of Pfannenstiel, Kroemer, Wilms, Arnsperger,[8] and others of recent date have appeared. A review of Bandler's work is found in *Progressive Medicine*[9] of June, 1902, so that it will be unnecessary to go into detail concerning it here, but simply to mention that he tries to prove the origin of these cysts to come from the remains of the Wolffian duct and misplaced ectodermal cells.

The cause of this apparently spontaneous segmentation on the part of the ovum is an unsolved problem, as is the cause of the proliferation of certain other cells to tumor formation; but the process is considered to be an analogous one by some of the recent investigators on the subject.

Arnsperger[8] says: "The fact that the maximum for the frequency of dermoids coincides with the height of the sexual life is important. This fact then speaks more for the derivation of ovarian dermoids from the ripe ova. I believe that if all dermoids (of the ovary) were congenital, more would be found at the autopsies of children."

It is significant that in many cases of so-called dermoids of the ovary there have been various other cysts and new-growths in combination with them.

Klein[10] states that 14 per cent. of the ovarian embryomata are combined with other types of cysts of the ovary. He reports one case in which a threefold combination was present in the same ovary, namely, an embryoma, a colloid cystoma, and a malignant tumor. Niemer[11] also reports several cases of combination of dermoids with other cysts of the ovary.

A case of Simmerling[12] has been reported, in which a proliferating glandular ovarial cystoma was found complicated with a small carcinomatous dermoid cyst.

Pfannenstiel[13] goes further and says: "The same impulse which causes the production of malignant tumor formation induces the formation of the dermoid cyst. From the epithelium of the Graafian follicle develops a simple cystoma or a pseudomucin cyst." He says, in another place, that ovarian dermoids are most frequently found combined with pseudomucin cysts.

Wilms[14] says that when we bring the two tumor groups in relation to each other, the embryomata of the testis and the embryomata of the ovary, with tumors in general, then we must consider them the most complex of all tumors. In his last contribution to the subject Wilms* defines the so-called dermoid cyst of the ovary as follows: "The embryoma of the ovary is a tumor composed of a threefold germinal anlage ultimately derived from an ovum, which, during its development in a small cyst, is early arrested, and only succeeds to the rudiment of an embryo."

Technique. When the macroscopic description of the first specimen was begun it became evident that it would be very much simpler to record the gross appearances of these bizarre tumors by means of

* M. Wilms' definition of the embryo: "Das Embryome des Eierstockes ist eine aus einer dreiblättrigen Keimanlage in letzter Instanz, also aus einer Eizelle hervorgegangene Geschwulstbildung, welche durch die Entwickelung in einer Kleinen Cyste in ihrem Wachsthum frühzeitig gehemmt, nur zu einem Rudiment eines Embryo auswächst."

sketches and photographs than by long verbose protocols; for in each instance there was an individual anatomy to deal with and no standard for comparison. Therefore, liberal use of the camera supplemented by explanatory sketches was employed throughout the study of them. The accompanying illustrations are some of the many views taken.

Since bone and teeth composed such a large part of the tumors, X-ray photographs of the specimens were taken in order to obtain the quantity and relation of the bone to the soft parts, and in each of them teeth hidden either in the bone or soft tissues were discovered. This proved of great value when it came to dividing up the material for microscopic study, and was the means of saving many a microtome knife; for, by comparing the specimens with the X-ray plate, one could tell exactly the points where to expect buried teeth and dense bone. Such pieces were left for a longer period in the decalcifying fluid.

On account of the close relationship of the bone, which was present in large masses, to the soft parts, it was necessary to decalcify the former without injury to the latter.

Most of the methods of decalcifying teeth and bone in large pieces, found in the various books on laboratory technique, do not give perfectly gratifying results in all respects. Either the bone is sufficiently decalcified and the staining characteristics of the soft tissues sacrificed, or the bone remains too hard to cut, and the soft parts are preserved. The weak solutions of acids take entirely too much time in the routine preparation of large pieces of bone for microscopic study, and daily changing of the decalcifying fluid is necessary over a period of several months. The use of phloroglucin as a protective with very strong acid is expensive, on account of the comparatively high price of phloroglucin as a laboratory reagent, and a long period of washing is necessary to remove the excess of acid, so that this method is not altogether satisfactory for large pieces of bone.

The ideal method for decalcifying bone and teeth, then, is one in which the insoluble organic salts may be removed in a short period of time, leaving the soft organic structures in their natural forms without marring the staining properties of the cells.

In preparing the above specimens for microscopic study the following steps were taken:

1. The specimen was hardened *en masse* by placing it in Orth's fluid for three to four days.

(Orth's fluid = Müller's fluid plus 4 per cent. formaldehyde.)

2. Washed in running water for twenty-four hours to remove the excess of this fluid, since a dark brown precipitate occurs in tissues left too long in Orth's fluid.

3. Removed from the running water and placed directly in the following decalcifying fluid:

Pure nitric acid from 75 c.c. to 100 c.c. (according to the density and size of bone, and the speed desired in decalcification); alcohol (95 per cent.), 750 c.c.; distilled water, 250 c.c.; sodium chloride, 7½ grammes.

This is a slight modification of von Ebner's decalcifying fluid.

The fluid was made up in this manner in quantities. The specimen was placed in a glass jar fitted with a tight screw top, to prevent loss of the alcohol, containing from 150 c.c. to 200 c.c. of this fluid at a time, according to the size of the specimen. The fluid was changed on an average of every four to five days until complete decalcification was obtained. This was ascertained by thrusting a fine needle into the portions of the specimen where the X-ray shadows indicated the firmest bone and teeth.

4. The specimen was transferred from the decalcifying fluid to the alkaline neutralizing fluid, composed of: aqua ammoniæ fortior, 10 c.c.; alcohol absolute, 90 c.c. It remained in this fluid twenty-four hours.

5. Alcohol and ether in equal parts.

6. Embedding in celloidin as usual, etc.

The results obtained by this method were very gratifying, not only in the sections obtained of the above specimens, but also of bone from other sources, such as osteomyelitis, epiphysitis, and teeth. The advantages of this method are in a general shortening of several of the steps usually taken in decalcifying, the uniformity in which the decalcification takes place, and the perfectly retained staining properties of the soft tissues.

It will be noticed that after hardening in Orth's fluid and washing in water the specimen is transferred directly to the decalcifying fluid. By the other methods usually employed the partial softening and swelling of the tissues incident to washing after Orth's fluid has to be overcome by a second hardening in alcohol before the decalcification process is begun. This, of course, takes time.

By using a decalcifying fluid that contains a high percentage of alcohol this is not necessary, for the alcohol in the decalcifying fluid serves as a hardening reagent to the soft parts, while the solid inorganic salts are attacked by the acid. Also, the presence of the NaCl in a quantity sufficient to bring the density of the fluid to about that of normal salt solution is a great protection to the soft parts, since it prevents the setting in of strong diffusion currents through the tissues, and the imbibition of water which would tend to swell and distort the cells.

Instead of removing the excess of acid by a prolonged washing of the specimen in running water, as is usually the custom, it is transferred immediately to a stronger alcoholic solution made alkaline by ammonia.

This is not only a saving of time in this step of the process, but also makes it unnecessary to submit the tissue to the dangerous process of too long washing and swelling of the decalcified tissues by imbibition. Ordinarily after such washing the specimens have to be rehardened by carrying them through graded alcohols before embedding. I believe that tissues are almost as frequently spoiled in decalcification processes by transferring them from alcoholic to aqueous solutions, and in and out of hardening and decalcifying fluids of different osmotic equivalents, as they are by too long contact with acids, or by using too strong acid solutions. The above decalcifying fluid varies from von Ebner's fluid in the use of HNO_3 instead of HCl, and in different proportions of the other ingredients.

By using an ammoniacal strong alcoholic solution to neutralize the excess of acid much time is saved, and the specimen is kept continually in a hardening fluid from the time it leaves its initial washing following Orth's fluid. The use of ammonia is preferred also to that of other alkaline reagents, such as $CaCO_3$, $NaHCO_3$, etc., since it may be used in almost any desired concentration and excess without injuring the tissues and without introducing an alkaline reagent that might reprecipitate some of the mineral salts which have been dissociated by the acid, but which may still remain in the tissues.

The extreme solubility of most ammoniacal salts precludes this. Also, a mineral alkaline body, if left in the tissues in excess, would interfere with the subsequent staining, since tissues should be neutral in reaction, in order to obtain satisfactory histological stains. The excess of ammonia, however, completely evaporates by the time the specimen has been carried through the alcohol and ether and embedding process and has been sectioned ready for staining. In several cases after the sections had been cut they were placed in a bottle with a small quantity of water, and vigorously shaken, so that any excess of free ammonia would be washed from them. This wash-water was then tested with litmus paper, and was found to be neutral.

Another characteristic of this process is that when this specimen is transferred from the decalcifying fluid, containing the nitric acid, to the neutralizing fluid, containing the ammonia, a bright-yellow or orange color is given to the specimen. This color is due to the well-known xanthoproteic reaction, which takes place in proteid bodies when treated with these reagents. This color, however, does not in any way detract from the staining of the cytoplasm of the cells with eosin. In fact, in many of the sections advantage was taken of this color reaction as a contrast to the nuclear stain, and then only hæmatoxylin was used. Whether this yellow color will persist or not, as eosin will for a long time, is doubtful.

In describing Specimen 1, it was stated that the whole embryoma had undergone such profound hyaline degeneration as to prevent a satisfactory microscopic study of it. At first it was feared that this hyaline degeneration might be an artefact caused by the strong decalcifying fluid, so a portion of the soft tissues from the other half of the embryoma and cyst wall that had not yet been decalcified was cut from the bone and carried through in the ordinary manner for soft tissues without coming in contact with the decalcifying fluid as a control test. When this was cut and stained it was found to behave toward the staining reagents in the same manner as the portion that had been decalcified. This proved that the decalcifying fluids had nothing to do with the poor staining properties of Specimen 1, but that a true hyaline degeneration had taken place.

Specimens of bone and teeth from various sources, combined with more or less soft tissues, have been decalcified by this method in pieces of 1½ cm. square in less than three weeks, which would have taken at least six to eight weeks by the ordinary methods, and they have retained their staining properties perfectly.

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ADRENAL TUMORS.

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Although the literature on the subject of adrenal tumors is not an extensive one, it has seemed to me that it would be useful to collate it, and so render it more accessible to students, for it is a scattered one. Such a collation will be based upon the paper of Kelynack, which up to its time was the most useful and comprehensive one in existence. Since the time of its publication many new facts have been added to our knowledge of these tumors, and especially to our knowledge of the malignant growths, which makes it necessary to add to the above-mentioned paper, admirable as it is.

Writers on pathology have not, apparently, been impressed by the remarkable facts discovered in the peculiar tumors in these important organs, for the current text-books—English and German alike—mention few of the common or uncommon features of them. One reason for such a neglect is that the earlier, and the later writers, too, have been interested in the relation between changes in the adrenal glands and Addison's disease, with the result that the case reports are of little or no present value in a large number of cases. There are, however, a few papers which are of much importance in this connection, notably those of Rolleston and Marks, Ramsey, Kelly, and Jores.

In discussing adrenal tumors I shall first deal with the benign tumors and then with the malignant ones.

Benign Tumors. The benign tumors of the adrenals belong in by far the greater number of cases to one class, namely, the adenomata, but the following varieties have also been reported: fibromata, lipomata, neuromata, gliomata, angiomata, and cystomata.

Fibromata have been reported by Saviotti and Mattei, but there is some doubt as to the authenticity of the cases, the general opinion being that they are, in all probability, fibro-adenomata—a class of tumors which is very common, and in which any proportion may exist between fibrous tissue and parenchyma. Fibromata may, however, occur, but are very rare.

Lipomata likewise have been reported—notably one case by Byford—but here, too, the probability is that these cases are tumors simulating lipomata, but in reality being adenomata which have undergone extreme fatty degeneration—a process which is extremely common in the adrenal and especially so in the adenomatous tumors.

Gliomata have been recorded in the literature by Virchow and Marchand. Reports coming from such sources are to be looked on as

valuable; but if such tumors do occur they must be rare anomalies, and due to tissue misplacement, for at the present time there is no reason to suspect that the adrenals contain any epidermic elements which could give rise to gliomatous tumors. Indeed, it has been very clearly shown in the past year that the old idea that the medulla of the adrenal was a derivative of nervous tissue is entirely erroneous, and that ganglionic tissue takes no part in the organogenesis.

Neuromata are to be looked upon with much suspicion, and although several cases have been reported by Weichselbaum, Armanni, and Formad, it is a question whether these are not really cases that should be classed as fibromata. If there is an authentic case of neuroma of the adrenal it must be an excessively rare one, and must be derived from one of the ganglia near the gland.

Of the more complex tumors there are three general classes, namely, adenomata, cysts, and angiomata, and in this last class are included two varieties—hæmangiomata and lymphangiomata.

Adenomata in general belong in two categories as regards size and multiplicity in the same organ. The most common are the small multiple adenomata, the large single tumors being far less commonly seen.

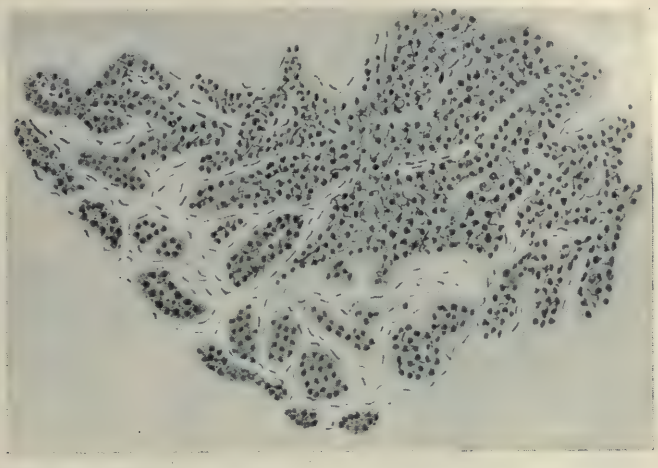
The small adenomata appear as yellowish nodules varying in size from a mustard-seed to a small pea. They occupy the medulla and the cortex, and are occasionally found just outside of the cortex, but beneath the capsule. In other words, they may arise in any zone of the organ.

When these are examined microscopically they are seen to be composed of cells which appear like adrenal cells affected by an advanced grade of fatty degeneration.

The larger adenomata—which occur singly, but occasionally bilaterally—show in their simpler forms a structure similar to that of the small adenomata, and their cells show the same tendency to fatty change. They usually originate in the cortex of the organ, and while they may form large tumors, they never involve the whole gland, and are usually seen as nodules projecting above the surface of the organ which they occupy. Their structure is more complicated than that of the small adenomata, and the arrangement of their columns of cells may become very intricate, as is the case in any other adenomatous tumor. As they increase in size the cells in the centre of the tumor undergo more or less fatty degeneration, and this process may extend to the supporting tissues, until the centre breaks down to form a cyst with mushy contents, or hemorrhage occurs into the softened tissue, forming a hemorrhagic cyst. By a gradual increase in the hemorrhage a huge cyst may at length be produced, similar to the one reported by Pawlik, which contained 10 litres of bloody material. In such a way, I believe, all the blood cysts of the adrenals arise, for hemorrhage into these

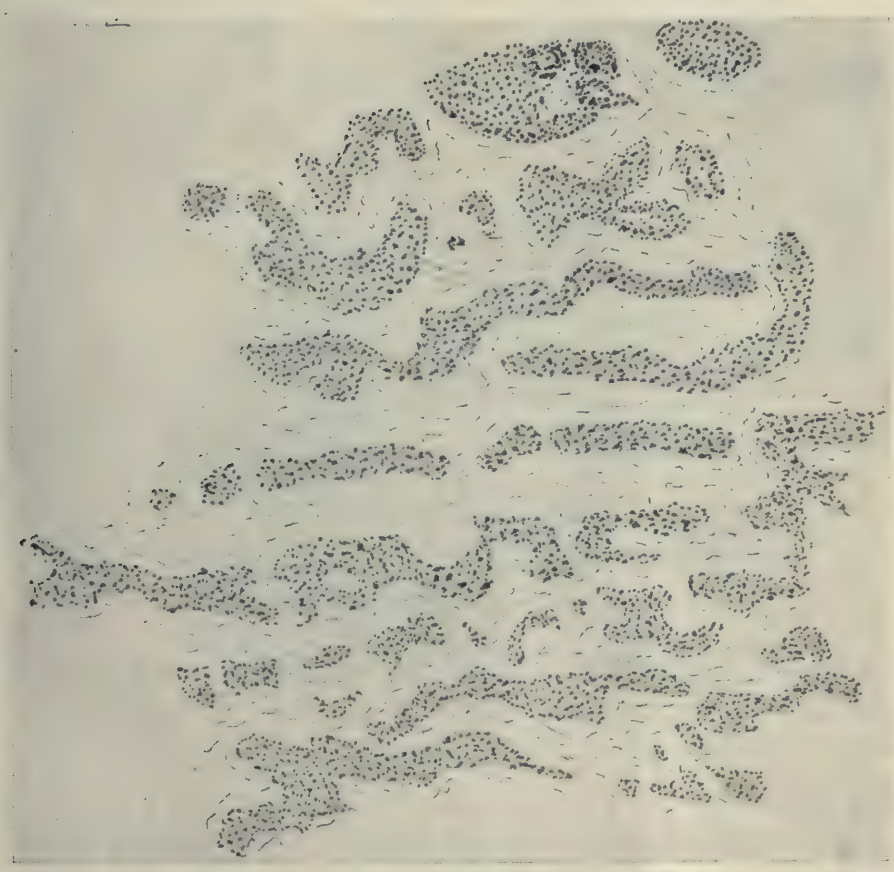
adenomata, and indeed into the glands themselves, is not a remarkably uncommon occurrence.

FIG. 1.



Case of cystic fibro-adenoma of adrenal. Zona glomerulosa in the wall of the tumor. Leitz eye piece IV., ocular 3. (Camera lucida.)

FIG. 2.

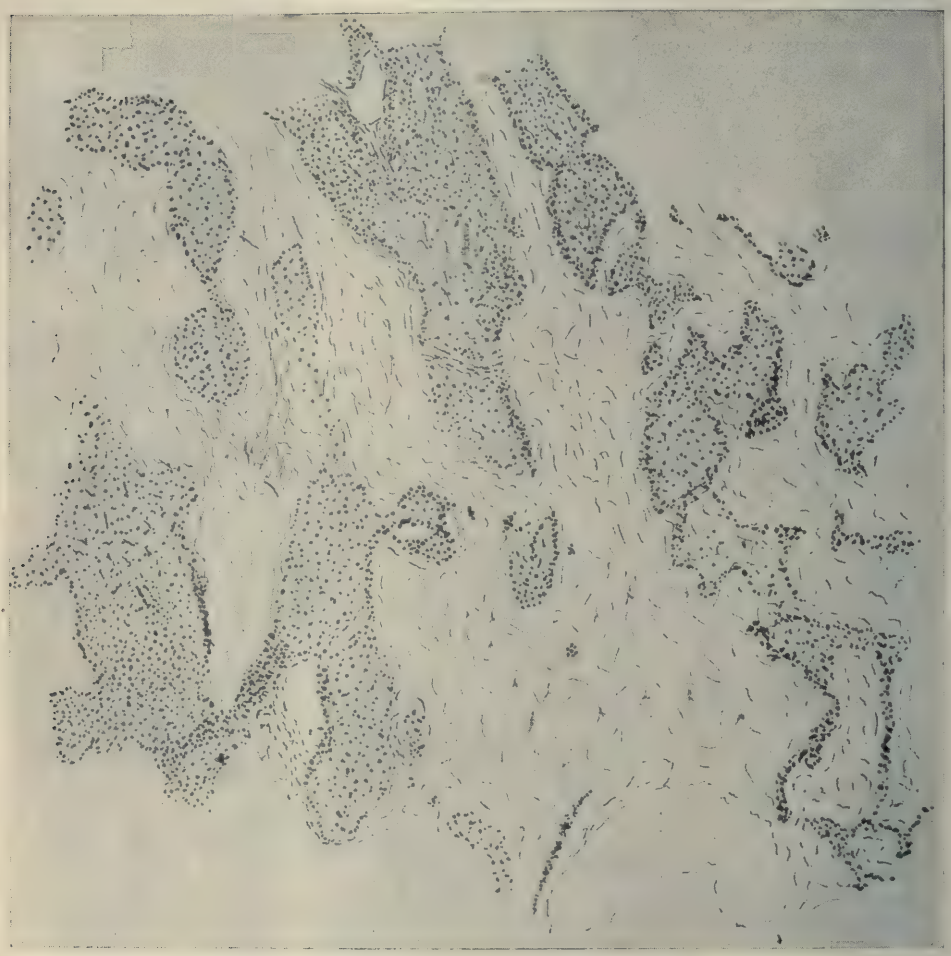


Zona fascicularis in wall of the tumor. Same magnification.

But besides these degenerative changes others may occur, and the resulting tumors have furnished the occasion for the reports of Letulle and Pilliet on "Surrénalites Nodulaires Hyperplastiques" and "Scléroses." In these so-called hyperplastic tumors there has apparently been an increase of the fibrous tissue, so that they come under the head of fibro-adenomata of more or less well-marked types.

The features of such tumors will be most easily remarked, I think, if I describe in some detail a tumor which came into my hands through

FIG. 3.



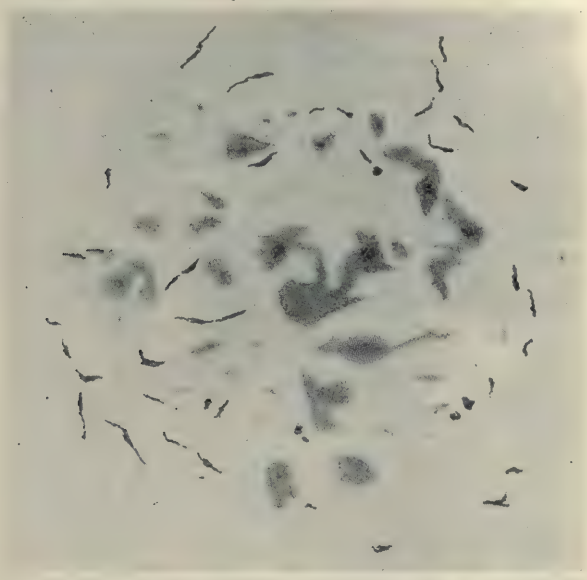
Zona reticularis in wall of tumor. Same magnification.

the kindness of Dr. McCrae, of the Montreal General Hospital. The tumor was accidentally discovered at autopsy, and nothing in the man's history can be shown to be due to the presence of the tumor.

The right adrenal, in which the tumor occurred, was somewhat larger than normal, even if the growth could be neglected, and at one end appeared a rounded protuberance, which was fairly firm and rather elastic. On section the gland itself was apparently normal. The

tumor, on section, presented a peculiar appearance. It was partially cystic, its contents being dark-brownish material, rather granular in appearance. The walls of the cyst were yellowish, with dark striations,

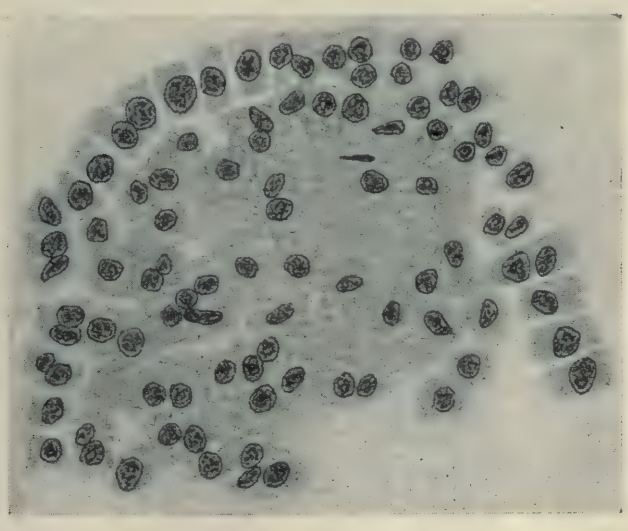
FIG. 4.



Areas of infiltration with lime salts. Leitz E. I., ocular 4.

and firm and tough. At one place there was an area that had the appearance of and cut like cartilage. To the apex of this area, which

FIG. 5.



Portion of a column of adrenal cells from zona fascicularis. Leitz E. IV., ocular 6. (Camera lucida.) The stain in all cases has been carbol-thionin.

projected into the cyst, was attached an arborescent mass of tissue, generally quite dark in color, which had the appearance of an intracystic papilloma.

On section of the wall of the cyst it was at once remarked that inside a compressed layer of fairly normal gland cortex was a fibroid and œdematous layer, composed of masses and columns of gland cells separated by masses of œdematous fibrous tissue, with occasional areas of pigmented material (the remains of old hemorrhage) and a few patches of calcareous deposit. (Figs. 1 to 5.) The area which had appeared like hyaline cartilage proved to be simply a hyaline fibrous tissue with a few nuclei, while the papillary, arborescent mass was the remnant of gland tissue which had not completely degenerated, and which had remained attached to fibrous strands and filled between with hemorrhagic detritus. This cystic fibro-adenoma was the size of a small English walnut.

Besides the hemorrhagic cysts two other varieties have been reported, namely, a serous variety by Ogle and a hydatid cyst by Bennett. This last, however, is a doubtful case, for in the description there are no details that would positively identify it.

Angiomata are rather rare growths, if we consider simply the benign forms, Klebs, Laboulbene, Vogel, and Seltz having reported cases. The case of Payne was a blood vascular tumor, while those mentioned by the other authors were lymphangiomata. They present no unusual features.

Malignant Tumors. When we come to study the primary malignant tumors of the adrenals we find a rather anomalous group of new-growths. The peculiarities of these tumors depend primarily upon the fact that they have their origin in a tissue that is less stable than epithelium or hypothelium, and which has been differentiated at a comparatively recent time, histogenetically, from the middle germ layer, and which is more closely related to the supporting tissues than are the two covering membranes of the body.

The adrenals are developed from the peritoneum—which in its turn has been a derivative of the middle germ layer—and of that division of mesoderm which we call mesothelium. This mesothelium seems to be the origin of tumors which at one time corresponded morphologically to the class of carcinomata, at another to sarcomata, and at another of a group of tumors which present a likeness to both the above types either in the same or in different nodules. Such tumors various authors have described in too little detail, and one such has furnished me with a text for a paper in which I have discussed at some length the changes which occur and the meaning of these variations. It will, therefore, suffice to mention here that the feature of greatest interest is the tendency for adrenal tumors of carcinomatoid appearance to form nodules, which may be purely sarcomatous or sarcocarcinomatoid, as the case may be. Rolleston and Marks and others emphasize this point.

As types of malignant tumors originating in the adrenals the following have been mentioned: carcinomata, sarcomata, endotheliomata, and peritheliomata.

In looking over the literature I have been unable to satisfy myself that the latter two varieties exist, although I have specimens of an aberrant adrenal tumor of the kidney that was distinctly a perithelioma; so these may exist also in the adrenal itself. If they do occur, and if they have the characteristics of the aberrant tumor that I have seen, they are tumors which show the ordinary characteristics of the malignant vascular tumors.

The other malignant tumors of the adrenals fall into two classes as they are described—*i. e.*, sarcomata and carcinomata. This classification rests, of course, on purely morphological grounds—a basis which is absolutely inadequate, White to the contrary notwithstanding—for many reasons, which I have discussed and which are sufficiently obvious. In my paper I described the tumor that I was studying as mesothelioma.

These adrenal mesotheliomata—or mesolepidomata, as Adami calls them—occur as large or small tumors, circumscribed or infiltrating, and originate in one of the zones of the cortex of the adrenal gland. When circumscribed they metastasize chiefly by the bloodvessels, but also by the lymph vessels in a certain number of cases. When they are infiltrating they may involve any of the neighboring organs, chiefly the liver and kidney, and are especially prone to invade the inferior vena cava. When small they may give rise to no symptoms that aid diagnosis, but they may give rise to many and serious symptoms by their metastases. The larger tumors produce various symptoms of tumor—such as a palpable, movable, or fixed mass in the renal region—and especially to symptoms of venous obstruction, due to pressure on, or thrombosis of, the vena cava. Metastasis, as a rule, occurs by the bloodvessels, and is most common in the liver and lungs. In twenty-two cases which I have collected from the literature which can be called carcinomata by the postulates of Rolleston and Marks there were metastases, as follows:

Liver	13 times.	Pericardium	1 time.
Lungs	11 "	Endocardium	1 "
Lymph glands	7 "	Uterus	1 "
Brain	3 "	Ovary	2 times.
Kidney	2 "	Spleen	1 time.
Peritoneum	3 "	Bones	2 times.
Appendix	1 time.	Diaphragm	1 time.
Stomach	1 "	Bladder	1 "
Mesentery	1 "		

These tumors occur at all ages. The youngest was nine months (Cohn) and the oldest seventy-three years (Ritchie and Bruce). In Ramsey's list of thirty-seven carcinomata[1] twenty-two were in men,

[1] It will be seen from these figures that Ramsey has given a longer list of primary carcinomata than I. This is because I do not feel that many of the cases quoted by him are primary, as judged by the rules of Rolleston and Marks, which I think are very useful and very logical, considering that "judgment is difficult."

and in my list of twenty-two, eleven were in men. I shall append a table of the cases of the carcinomatoid tumors judged by the postulates of Rolleston and Marks.

The microscopic appearances of the malignant adrenal tumors vary. I have seen none that show purely sarcomatous appearances, but, judging by some of the descriptions in the literature, they do occur. Indeed, they are the more common variety. They conform in appearance to other sarcomata, and are spindle-celled or round-celled in type. The carcinomatoid tumors have an alveolar appearance corresponding in a certain extent with the arrangement of the normal gland. In some instances they have a peculiar perivascular arrangement, which I think is uncommon.

The primary tumor may correspond to the carcinomata even in the arrangement of the reticulum, but there is a tendency for the reticulum to become intercellular even when in the larger part of the tumor it surrounds groups of cells. In the case which I described the reticulum in the primary tumor separated groups of cells, while in the metastases, in lymph glands, and brain it was intercellular. In the lungs the arrangement took on characters of the so-called carcinoma-sarcomatodes. The origin of these tumors has been shown to be, at least in some cases, in the parenchyma of the organs, and is not due to connective-tissue changes or to proliferation of the cells of the bloodvessels.

Finally, the cells of malignant adrenal tumors, like those of other malignant growths, are larger as a rule, the nuclei are larger comparatively, the protoplasm less in amount, and the nuclear substance more abundant than normal. Mitotic figures, regular and atypical, are common.

The most noticeable feature in these tumors is their well-marked tendency to variation in type, due to the remarkable inclination of the cells to metaplastic changes.

In the accompanying tabulation of the primary carcinomatoid adrenal tumors there will be found a brief epitome of the characters and clinical observations abstracted from the case reports. In the tabulation I cannot include the cases of Stybr and Nuno Porto, because I have not been able to read the first or obtain the second paper, and because I have been unable to find any adequate abstract of either case. It has, however, been asserted by several authorities that the first was a primary melanotic carcinoma, and that the second was also a primary growth.

Secondary Malignant Growths. Secondary tumors are not uncommon, and occur in persons past middle life in the great majority of cases. In looking over the autopsy records of the Royal Victoria Hospital I was able to find mention of secondary sarcoma in one case in fifteen; of secondary carcinoma in seven cases in forty-eight.

The case of sarcoma occurred in a case of multiple sarcoma, and nodules were found in both adrenals. The cases of carcinomata occurred as follows: cancer of the stomach with metastases in the left adrenal, three times; in the right adrenal, twice; cancer of the pancreas, in both adrenals, once; cancer of the bile-duct, in both adrenals, once; in the left, once; cancer of the intestines, in the right adrenal, once.

NOTE.—Since I have had the proofs of the preceding remarks, I have come across three interesting papers that had escaped my notice, in spite of my care in searching the literature.

One of these papers is that of Morris (*Brit. Med. Journ.*, 1899, vol. ii. 1336), which discusses three cases of adrenal growths, all of which the author considers to be sarcomata, although, as he says, the resemblance to carcinoma is a very marked feature in some cases of the growths. The first case has been recorded in the *Reports of the Middlesex Hospital* (1888, p. 230) as a "Sarcoma of the Adrenal." It occurred in a man, aged fifty-one years, and weighed 61½ ounces. The left adrenal only was involved. His second case was in a man, aged forty-three years, and in this instance the tumor was on the right side. No autopsy was obtained, and there is some doubt as to whether the growth was certainly primary in the adrenal.

The third case was that of a woman, aged forty-three years. In this case the growth was a cystic sarcoma, and after operation the patient died, with recurrences.

The second paper is that of Orr (*Edin. Med. Journ.*, 1900, vol. l.), who reports a case of sarcoma in a child, aged seven weeks. Both adrenals were affected. The liver was involved by the growth. Dr. Leith gives a good pathological discussion of the findings, and decides that the case is one of small round-celled sarcoma, although it could be distinguished only with some difficulty from carcinoma. This is the youngest case on record.

Three of these cases then deserve to be classed with the so-called "primary sarcomata," the other is possibly primary.

The third paper is that of Schnittenhelm (*Wien. klin. Rundschau*, 1901), and in this paper a case of medullary cancer of both adrenals in a man, aged fifty-five years, is described. This case may be one of primary carcinoma. The remarkable features of this case are the clinical symptoms, which Schnittenhelm ascribes to an auto-intoxication. There was no pigmentation.

Table of Primary Carcinomatoid Adrenal Tumors.

No.	Source.	Publication.	Sex and age.	Gland.	Nature.	Secondary growths.	Pigmentation.	Remarks.
1	Rolleston and Marks,	Amer. Journ. Med. Sci., n.s., vol. cxvi. p. 116.	Male, 50	Left.	Round-cell carcinoma.	Liver, peritoneum.	None.	Ascites; œdema of feet. Diagnosis: abdominal aneurism.
2	Ibid.,	Ibid.	Male, 40	Right.	Round-cell carcinoma.	Right and left lungs, liver, aortic glands.	None.	Pneumonia.
3	Ibid.,	Ibid.	Female, 52	Right.	"Malignant adenoma."	Liver.	None.	Anæmia; leucocytosis; emaciation; enlarged liver and spleen; kidney invaded; pleural effusion; ascites; œdema of legs.
4	Ogle,	Trans. Path. Soc., London.	Female, 3	Left.	"Malignant adenoma."	Liver.	"Gypsy color."	Constant vomiting; weight increased; pubic hair, moustache; colon depressed.
5	Ritchie, Bruce,	Edinburgh Med. Journ.	Male, 73	Both.	Carcinoma.	Lungs.	None.	Vomiting.
6	Weinburg, Turquet,	Bull. Anat. Soc., Paris.	Female, 36	Both.	Carcinoma.	Both lungs, cerebellum, appendix.	.....	Dilated stomach; diarrhœa; lumbar pain; vomiting; severe headache.
7	Fenwick,	See Rolleston and Marks.	Male, 62	Right.	Carcinoma.	Liver, mesentery, stomach; pancreas invaded by continuity.	None.	Pulsation (not expansile); left adrenal enlarged; vena porta and vena cava inferior thrombosis; six ounces of blood clot in tumor; blood-stained fluid in peritoneal cavity.
8	Brooks,	Redcliffe Infirmary.	Female, 49	Left.	Carcinoma.	Liver, lungs, right adrenal, bronchial glands.	None.	Irregular temperature; emaciation; pain down left leg.
9	Ibid.,	Roy. Col. Surg. Museum.	Female, 32	Right.	Carcinoma.	Liver and aortic lymph glands.	.....	Growth into vena cava inferior; hypertrichosis.
10	Carrière Délearde,	Arch. de Méd. Expér.	Male, 54	Both.	"Epithelieme atypique."	Liver, lungs.	None.	Palpable tumor; œdema of legs; cachexia; diarrhœa; pleural effusion; ascites.
11	Pawlik,	Arch. f. klin. Chirurgie.	Female, 50	Both.	Melanotic carcinoma.	Right kidney, brain, lungs, pleuræ, epicardium, endocardium, peritoneum, liver, and uterus.	.....	Extension of right kidney; loss of appetite; vomiting; increased urine; right facial paralysis; right pupil dilated; almost complete amnesia; right hemiplegia; urine and feces passed involuntarily.

12	Bruchanow,	Zeits. f. Heilkunde.	Female, 14 mos.	Right.	Medullary carcinoma.	Lymph glands, right ovary.	.....	Thrombosis inferior vena cava; œdema of feet; extension to liver.
13	.....	.....	Male, 63	Right.	Carcinomatous degeneration of a struma.	Liver and right lung; lymph glands.	.....	Extension to liver; œdema of feet; asthenia.
14	.....	....	Female, 66	Right.	Cancer.	Lymph glands; spleen.	.....	Growth in kidney a collateral development in accessory gland.
15	Orth,	Arbeiten Göttingen.	Female, 4½	Right.	Carcinoma.	Liver and lungs.	.....	Abnormally developed genitalia.
16	.....	....	Male, 49	Left.	Carcinoma.	Liver.	.....	Death from marasmus.
17	Marchand,	Virchow's Festschrift.	Female, 20	Right.	Carcinoma.	Left ovary, liver.	.....	Irregular menstruation; œdema of legs.
18	Collinet,	Bull. Anat. Soc., Paris.	Male, 53	Right.	Epithelioma.	Diaphragm, reno-cæcal ligament.	None.	Œdema of legs; loss of appetite; growth extended to liver and kidney; cells in portal vein.
19	Stoukoventoff,	Gaz. Méd. de Paris.	Female, 50	Both	Carcinoma.	Liver and lungs.	None.	Fever; pain over liver; liver enlarged; sanguineous expectoration; œdema of legs; albuminuria; dyspnœa; cyanosis.
20	Posselt,	Wien. klin. Woch.	Male, 46	Left.	Carcinoma.	Left lung, kidney, lumbar vertebræ.	Present.	Had pulmonary tuberculosis and Addison's disease; symptoms of these.
21	Kelly,	Ziegler's Beiträge.	Male, 68	Left.	Carcinoma.	Bladder and lungs.	.....	Metastasis by inferior vena cava.
22	Woolley,	Journ. Exp. Medicine.	Male, 42	Both.	Mesothelioma.	Right lung, brain, lymph glands.	None.	Fainting attacks; weakness; dyspnœa; incontinence of urine and feces; symptoms of meningitis; frontal headache; vomiting; optic neuritis.

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ON ADRENALIN GLYCOSURIA AND CERTAIN RELATIONS BETWEEN THE ADRENAL GLANDS AND CARBOHYDRATE METABOLISM.

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THE adrenal gland was for the first time brought into relation with glycosuria by F. Blum,[1] of Frankfort, who in September, 1901, published observations showing that extracts of the adrenal glands of sheep are capable of inducing a slight or moderate grade of glycosuria when injected subcutaneously into dogs and rabbits. The results of Blum were confirmed in Europe, and led in this country to experiments with Takamine's adrenalin chloride and Abel's adrenalin which have extended our information as to the glycosuria following the administration of preparations made from the adrenals. Herter and Richards[2]

[1] Ueber Nebennierendiabetes, Deutsches Archiv für klin. Medicin, Bd. lxxi.
[2] Medical News, February 1, 1902.

found that the intraperitoneal injection of solutions of adrenalin chloride is followed almost regularly by the presence of large percentages of sugar in the urine, and the present writers made a study of some of the conditions under which adrenalin glycosuria occurs.[1] In this paper it is desired to offer a summary of the more important observations that have now been made, in the belief that they are of interest as throwing new light on the physiology of carbohydrate metabolism.

General Description of Experimental Adrenalin Glycosuria. The intensity and duration of adrenalin glycosuria depend in part on the mode of administration, in part on the size of the dose. Subcutaneous injections yield less sugar than intravenous or intraperitoneal injections. Direct applications to the surface of the pancreas usually cause considerable excretion of sugar, even when the quantity of adrenalin used is small (say 1 c.c. solution of adrenalin chloride 1 : 1000). The slightest glycosurias in proportion to the dose have come from the use of adrenalin chloride by the mouth. Dogs of medium size may receive 10 to 20 c.c. of the commonly used adrenalin chloride solution (1 : 1000) without developing glycosuria; larger doses may be followed by a moderate or considerable glycosuria. This relative inertness of the substance when given by the mouth has a certain practical importance, and is readily explained. Adrenalin is very easily oxidized, and quickly loses both its blood-pressure-raising property and its ability to induce glycosuria. When introduced into the stomach the gastric epithelial cells have an opportunity to destroy a considerable portion of the active substance before it is absorbed. It thus loses a large part of its efficacy in raising the blood pressure. It is preferable to give adrenalin subcutaneously to giving it by the stomach, for, in addition to securing greater precision and economy in dosage, this method has the advantage of avoiding any ill effects upon the stomach. We have never known the usual dose for subcutaneous use

[1] Table Showing Effect of Intraperitoneal Injection of Adrenalin of Dilution 1 : 1000.

Weight of dog.	Amount of solution used.	First catheterization after	Sugar.	Second catheterization after	Sugar.	
18.6 kilo.	9 c.c.	1 hour.	5.0 per ct.			
21 "	10 "	.....	1.0 "			
8.2 "	7 "	1 hour.	10.0 "			
11.3 "	10 "	1 "	5.3 "			
10.9 "	10 "	30 min.	5.0 "	1 hr. 30 min.	6.5 per ct.	
13.2 "	11.5 "	2 hr. 30 min.	5.0 "	3 " 10 "	7.33 "	
10 "	5 "	40 min.	6.11 "	2 " 20 "	11.5 "	
5 "	2 "	4 hours.	3.75 "			
6.8 "	10 "	.....	4.8 "			
8.2 "	5 "	.....	1.25 "			
7.3 "	5 "	.....	2.7 "			
7.3 "	10 "	1 hr. 25 min.	2.0 "	6 hr. 30 min.	4.2 per ct.	Abel's adrenalin.
6.4 "	10 "	1 " 10 "	7.15 "	.....	.....	" "

(0.3 to 1.2 c.c.) to occasion glycosuria, even when repeated at intervals of three or four hours.

The degree and duration of the glycosuria vary widely in different animals, and sometimes in the same animals at different times. Intraperitoneal injections of 5 c.c. of adrenalin chloride in normal dogs of medium size (8 to 15 kilos) almost without exception cause the appearance (within one or two hours) of a glycosuria, with from 3 to 10 per cent. of sugar in the urine. The duration of the glycosuria following a single dose is seldom longer than thirty hours. During this time there is a total excretion of glucose which does not commonly exceed 2 or 3 grammes. The amount of sugar which appears during and after frequently repeated doses of adrenalin may greatly exceed these amounts. For example, this is well shown in the following experiment, in which the pancreas was repeatedly painted with adrenalin:

Experiment. Normal dog; weight, 13.6 kilos; well nourished. Meat diet. Bladder emptied; urine normal. Lacteals found distended. Pancreas divided into two nearly equal parts. Adjoining duodenum also cut through transversely. Between 10.45 A.M. and 9.25 P.M. head end of the pancreas painted ten times with 1 c.c. adrenalin chloride solution (1 : 1000). Slightly under ether throughout the entire experiment.

Urine,	first	catheterization	12.35 P.M.,	70 c.c.,	7.25	per cent.	sugar.
"	second	"	2.15	"	60 c.c.,	14.3	"	"
"	third	"	3.15	"	48 c.c.,	12.5	"	"
"	fourth	"	4.30	"	25 c.c.,	9.75	"	"
"	fifth	"	5.50	"	14 c.c.,	6.0	"	"
"	sixth	"	7.00	"	10 c.c.,	2.22	"	"
"	seventh	"	8.00	"	6 c.c.,	1.82	"	"
"	eighth	"	9.00	"	7 c.c.,	1.4	"	"
"	ninth	"	10.15	"	4.5 c.c.,	0.83	"	"

The total quantity of sugar excreted during this experiment was 23.4 grammes (estimated as glucose). The observation is instructive not merely in showing how high a grade of glycosuria may be caused by the action of adrenalin, but also as indicating how small a quantity of adrenalin is capable of calling forth so great an amount of sugar. The amount of adrenalin substance employed in this experiment was approximately 0.01 gramme. We do not know of any form of experimental glycosuria in which such pronounced effects can be obtained with so small a quantity of toxic material.

The susceptibility of different dogs to adrenalin varies considerably so far as glycosuria is concerned. One sometimes finds animals which do not show any glycosuria whatever, even after one or more applications to the pancreas.[1] The differences noted appear to be connected with the state of nutrition, and especially with the quantity of gly-

[1] Many of our animals showed themselves insusceptible to the action of piperidin in causing glycosuria, while others excreted very large quantities of sugar. This difference appeared to be largely independent of the size of the dose applied to the pancreas.

cogen which is stored in the organism. It appears doubtful, however, if these differences in susceptibility can be accounted for wholly in this way. It seems to us that there are other factors of which the nature is unknown.

In adrenalin glycosuria the sugar of the blood is regularly increased but falls rapidly with the decline in the sugar of the urine, and after a time may drop below the original normal level. In respect to the increase of blood sugar adrenalin glycosuria resembles the majority of cases of human diabetes, and differs from the experimental glycosuria after phloridzin, where the sugar-content of the blood is commonly lower than normal. The volume of the urine in adrenalin glycosuria is usually distinctly increased. The presence of diacetic acid or oxybutyric acid has not been observed. The occurrence of glycosuria from adrenalin is wholly independent of any change in the general blood pressure, as was shown in experiments where sugar occurred in the urine in spite of a marked fall in carotid blood pressure from nitroglycerin.

Physiological Characters of Adrenalin Glycosuria. One of the first questions that arises relates to the origin of the sugar which appears in the urine. This sugar might be thought of as coming either from an increased conversion of hepatic glycogen or from a diminished combustion of sugar. In favor of the former view are two facts—first, the decline in the glycogen store of the liver during adrenalin glycosuria; and, secondly, the increased sugar-content of the blood of the hepatic vein as compared with the blood of the portal vein. The following table gives three typical observations made by Dr. Richards upon the sugar of the blood of the femoral artery, portal vein, and hepatic vein, before and after treatment of the pancreas with adrenalin. The collections of blood were made simultaneously by means of specially designed canulæ.

These figures call for little comment. In two of the three observations the sugar of the blood of the femoral artery, portal vein, and hepatic vein showed a fairly close correspondence before the application of adrenalin. In the third case the blood sugar of the hepatic vein was considerably lower than that of the blood of the portal vein. In all three cases the percentage of blood sugar of the hepatic vein rose quickly to a point in excess of the percentage in the portal vein, and remained so during the subsequent observations. It is safe to infer that this behavior of the blood sugar is referable to the increased production of sugar within the liver.

TABLE SHOWING PERCENTAGE OF SUGAR IN BLOOD BEFORE AND AFTER TREATMENT OF PANCREAS WITH ADRENALIN.

Weight of dog.	Starved.	Blood drawn at	Pancreas painted at	Sugar in blood from		
				Femoral artery.	Portal vein.	Hepatic vein.
8.2 kilo.	48 hours.	3.50 P.M.	.....	0.142 per ct.	0.148 per ct.	0.143 per ct.
		.....	4.04 P.M.			
		4.08 P.M.		0.191 "	0.151 "	
		4.21 "		0.179 "	0.154 "	0.177 "
		5.07 "		0.132 "	0.107 "	0.130 "
9.2 kilo.	24 hours.	4.23 P.M.	.....	0.160 per ct.	0.165 per ct.	0.164 per ct.
		.....	4.39 P.M.			
		4.49 P.M.		0.247 "	0.197 "	0.284 "
		5.20 "		0.322 "	0.245 "	0.346 "
7.8 kilo.	20 hours.	4.21 P.M.	.....	0.159 per ct.	0.169 per ct.	0.136 per ct.
		.....	4.40 P.M.			
		4.44 P.M.		0.187 "	0.167 "	0.201 "
		5.06 "		0.215 "	0.187 "	0.252 "
		4.46 "		0.208 "	0.207 "	0.209 "

In what way adrenalin occasions an excessive conversion of glycogen into sugar is still undecided, but there are some experimental observations that have to be considered in any attempt to form a judgment on this question. One of these is that applications of small amounts of adrenalin to the surface of the pancreas or injections into its substance have given rise to a more pronounced glycosuria than similar procedures in the case of the brain, liver, spleen, or kidney.[1] This suggests that in the production of glycosuria adrenalin acts especially, if not exclusively, upon the cells of the pancreas; but it has been impossible to prove that the action of adrenalin depends wholly on the presence of the pancreas, for total extirpation of this gland is quickly followed by an excretion of sugar.[2] Another difficulty arises from the fact that since adrenalin acts when introduced into the circulation, the substance may find its way to other organs when applied to the surface of the pancreas. If, however, it could be shown that there are substances which are capable of inducing glycosuria when painted on the pancreas, but do not cause it when introduced into the circulation or into the brain, spleen, or liver, we should have strong evidence that the substances in question when applied to the pancreas act on this organ only. A substance of this nature is potassium cyanide. The action of this poison in its relation to glycosuria is illustrated by the following tables:

[1] No observations of this kind have as yet been made upon the adrenal bodies.

[2] It is possible that some information could be obtained after total extirpation of the pancreas by making intraperitoneal injections of adrenalin when the quantity of sugar excreted from hour to hour is small and fairly constant.

TABLE SHOWING EFFECT OF APPLYING POTASSIUM CYANIDE SOLUTIONS TO PANCREAS.[1]

Weight of dog.	How applied to pancreas.	Amount of solution used.	Strength of solution.	Duration of application.	First catheterization after	Volume of urine.	Sugar.	
.....	Painted.	2 c.c.	$\frac{N}{1000}$	.....	1 hour.	.....	2.1 %	
4.5 kilo.	Painted.	3 "	"	30 min.	1 h. 40 m.	2 c.c.	'strong'	
6.8 "	Painted and injected.	2 "	"	10 "	1 hour.	9 "	0	
9.5 "	Painted and injected.	2 "	"	.....	30 min.	.....	6.0 %	Applicati'n to tail of pancreas.
7.2 "	Painted.	1.5 "	"	13 min.	2 hours.	5 "	1.5 %	
9.1 "	Injected.	3 "	"	.....	2 "	4 "	trace.	
11.8 "	Painted and injected.	3 "	"	10 min.	1 hour.	9 "	0	
10.4 "	Injected.	3 "	"	10 "	2 h. 45 m.	65 "	0.25 %	Applicati'n to head of pancreas.
6.8 "	Painted and injected.	2 "	"	10 "	2 hours.	8 "	trace.	
5.4 "	Painted and injected.	2 "	"	.....	4 h. 45 m.	7 "	trace.	

TABLE SHOWING EFFECT OF INTRODUCING POTASSIUM CYANIDE SOLUTIONS INTO A MESENTERIC VEIN OR INTO THE FEMORAL VEIN.

Weight of dog.	Where injected.	Amount of solution injected.	Strength of solution.	Duration of injection.	First catheterization after	Volume of urine.	Sugar.
9.1 kilo.	Into mesenteric vein.	3 c.c.	$\frac{N}{1000}$	.....	1 h. 10 m.	.....	0
10 9 "	" "	6 "	"	.....	.....	.....	0
6.8 "	" "	10 "	"	2 min.	2 hours.	13 c.c.	0
4.5 "	" "	14 "	"	2 "	2 h. 15 m.	35 "	0
8.2 "	" "	250 "	"	60 "	2 h. 10 m.	0	
7.7 "	" "	85 "	"	.....	2 h. 15 m.	23 c.c.	0
7.3 "	Into femoral vein.	5 "	"	25 min.	2 hours.	5.5 "	0
7.7 "	" "	3 "	"	30 "	2 hours.	12 "	0
9.1 "	" "	6 "	"	15 "	1 h. 30 m.	25 "	0
7.3 "	" "	200 "	$\frac{N}{100}$	.....	.....	.....	0
6.4 "	" "	200 "	$\frac{N}{750}$	60 min.	30 min.	4 c.c.	0

It is apparent that a dilute solution $\left(\frac{N}{1000}\right)$ of potassium cyanide when applied to the surface of the pancreas is capable of inducing a glycosuria of slight degree, which is dependent not on the transportation of this poison to some distant part by means of the blood, but on its direct influence on the cells of the gland. There is, of course, no evidence that there are not other cells in the body which react to

[1] The animals were in almost every instance fed on lean meat.

hydrocyanic acid in such a way as to provoke glycosuria; but experiments made upon the cerebral cortex, the liver, the spleen, and the decapsulated kidney gave negative results. These various experiments with potassium cyanide, in connection with the observed sensitiveness of the pancreas to local applications of adrenalin, point to the pancreas as the part chiefly concerned in the production of adrenalin glycosuria, although here, again, there is no proof that some cells other than those of the pancreas do not possess a similar sensitiveness.

How the application of adrenalin to the pancreas initiates those hepatic changes which result in glycosuria is not yet clear. We at one time thought it possible that during the glycosuria something leaves the pancreas by the pancreaticoduodenal vein which stimulates the conversion of glycogen into sugar. Experiments designed to test this idea did not give it any support. At present it appears much more likely that the glycogenetic function of the liver is stimulated through the mediation of the sympathetic nervous system. No direct investigation of this phase of the subject has yet been made.

As to the way adrenalin acts on the cells of the pancreas there is no positive information, although there are two considerations which led us to conclude that the disturbance of function is of a kind that involves impaired oxidation within the pancreatic cells. One of these is that hydrocyanic acid has the property of interfering with the capacity of cells to appropriate oxygen, as was shown conclusively by the work of Geppert. It is conceivable that hydrocyanic acid has other properties which contribute to render it poisonous, but the interference with oxidation seems to sufficiently account for its powerful toxic action. It is therefore reasonable to assume that the ability of potassium cyanide to cause glycosuria is due to interference with the appropriation of oxygen by the pancreatic cells. It is possible that this disturbance in oxidation makes itself felt in an action upon the nerve-endings in the pancreas, resulting in the hepatic overaction already mentioned in speaking of adrenalin glycosuria.

What we know about the action of hydrocyanic acid led us to inquire whether there are not other poisons that have a similar action upon cells in respect to interference with intracellular oxidations. It was found that there are many substances which lead to glycosuria when applied directly to the pancreas. Comparing these with respect to their ability to oxidize or reduce, it was found that substances which exert a reducing action are more likely to induce glycosuria than those which have an oxidizing action. It must be admitted, however, that it has been possible to experiment with only a relatively small number of oxidizing and reducing agents, and that a wider experience may not sustain the generalization that the property of inducing glycosuria belongs much more to reducing than to oxidizing substances. On the

other hand, the results obtained up to the present cannot be ignored. It is impracticable to give these results in detail here, but some facts regarding them should be mentioned. Thus it was found that substances which reduce Fehling's solution occurred in the urine after the application of the following poisons to the pancreas: sulphurous acid, sulphuretted hydrogen, carbon monoxide, benzyl alcohol, and pyrogallol. Experiments with common oxidizing agents gave results quite different from those obtained with the reducing agents just mentioned. Chlorine-water (saturated solution), bromine-water (saturated solution), potassium chlorate (10 per cent. solution), hydrogen peroxide (saturated solution, fresh), chromic acid (2 per cent. solution), and nitric acid (2 per cent. and 10 per cent. solutions) all yielded negative results when painted on the pancreas. Among the oxidizing agents tried, only nitrobenzol (4 per cent. to 10 per cent. solutions) gave sugar, but a more thorough search would doubtless reveal others which have this effect.

Among substances which have little or no reducing action, but produce glycosuria, may be mentioned sodium salicylate[1] (50 per cent. solutions) and potassium cyanide. On the other hand, sodium thiosulphate (10 per cent. to 90 per cent. solutions), a powerful reducing agent, wholly failed to induce glycosuria.

It is thus clear that we cannot attribute the experimental glycosurias that have been observed merely to the reducing properties of the substances employed, but rather to some obscure toxic action exerted probably on the cells of the pancreas.[2] What we know of the action of potassium cyanide indicates that this toxic action involves interference with intracellular oxidation.

It seemed possible at first that experimental adrenalin glycosuria might be referable to a temporary inhibition of that function of the

[1] TABLE SHOWING EFFECT OF APPLYING SODIUM SALICYLATE SOLUTION TO PANCREAS.

Weight of dog.	How applied to pancreas.	Am'nt of soluti'n used.	Strength of solution.	Duration of application.	First catheterization after	Vol. of urine.	Sugar.	Remarks.
12.7 kilo	Painted.	1 c.c.	50 %	15 min.	2 hours.	13 c.c.	2.0 %	
7.7 "	"	2 "	"	25 "	2 "	16 "	3.8 %	
7.7 "	"	1 "	"	15 "	3 "	25 "	0.2 %	
.....	Injected.	5 "	"	.....	1 h. 50 m.	4½ "	0.3 %	
9.1 kilo.	"	2 "	"	.....	2 hours.	12 "	2.8 %	
10.4 "	Painted.	1 "	"	7 min.	1 h. 30 m.	.....	9.0 %	Application to tail of pancreas.
5.4 "	"	½ "	"	30 "	2 h. 30 m.	18 c.c.	8.5 %	Application to head of pancreas.

[2] There is no direct evidence that these substances act only on the pancreas, but the cyanide experiments suggest that this may be the case. We hope to have the opportunity to test this question individually with the different poisons that occasion glycosuria.

pancreas which normally prevents the excretion of sugar, but this view soon became untenable for the following reason: If one cuts transversely through the pancreas and duodenum, so that the severed portions of the organ have their only vascular connection through the general circulation, the application of a weak potassium cyanide solution to either portion of the gland is still liable to induce glycosuria. We know from experiments already mentioned that potassium cyanide injected into the circulation failed to cause glycosuria; hence we are justified in assuming that when the cyanide acts on one part of the divided pancreas it has no influence upon the remaining portion, but acts wholly by means of this local action. As it is well known that dogs with one-half the pancreas intact do not develop glycosuria, it is evident that we have in the phenomena of cyanide glycosuria something distinct from the glycosuria that follows extirpation of the pancreas.

When the pancreas is divided in the manner just mentioned the application of a small quantity of adrenalin chloride (1 c.c. of a 1 : 1000 solution) to either end of the gland is generally followed by glycosuria. We know that when adrenalin is injected into the circulation it is capable, unlike dilute solutions of potassium cyanide, of inducing glycosuria; hence this method of experimentation does not enable us to exclude some action of adrenalin upon the unpainted part of the gland and upon other organs, yet the cyanide experiment makes it highly improbable that such action upon the unpainted gland is necessary for the production of glycosuria.

We have at present no indication whether an application of potassium cyanide or adrenalin to the pancreas acts chiefly upon the secreting glandular cells, the cells of the islands of Langerhans, or the nerve endings in the pancreas. As the islands of Langerhans have been shown by Opie to be somewhat more numerous in the tail of the dog's pancreas than in other parts, it was thought desirable to make a series of observations in which the caudal half of the organ was painted with adrenalin, and a second series in which the cephalic and descending half of the gland was so painted. There are fifteen observations in each series. As regards the weights and feeding of the dogs and the operative conditions of the experiments, the two series of observations are comparable. The pancreas was in each case severed into two approximately equal parts, the duodenum being also cut through. The amount of adrenalin chloride solution (1 : 1000) varied from 1 c.c. to 2 c.c., according to the weight of the animal. The time required for the application of the adrenalin solution was usually fifteen or twenty minutes. The urine was collected hourly by catheter for three or four hours after the paintings. Considerable variations in the degree of glycosuria were, as usual, noticeable in different animals. The total excretion of

sugar noted in fifteen dogs of the first series, in which the tail half of the pancreas was painted, was 17.25 grammes. The total excretion of sugar by the fifteen dogs of the second series, in which the cephalic half of the gland was painted, was 15.60 grammes. It cannot, of course, be maintained that these results prove the caudal end of the pancreas to be more sensitive to the action of adrenalin than the cephalic half. To determine whether this is actually the case much more numerous observations would have to be made. On the other hand, the results of our experiments are in no way opposed to the possibility that adrenalin exerts its influence through the islands of Langerhans—a possibility which naturally suggests itself, although there is no proof that adrenalin acts exclusively on the pancreas in the production of glycosuria. Some light may perhaps be thrown on this question by a study of the histological conditions in the pancreatic glands of animals that have been treated with intraperitoneal injections of adrenalin through a long period of time.

It has not been possible to induce a permanent glycosuria by means of repeated intraperitoneal injections; but in one dog in which such injections had been made at short intervals during five weeks, with a glycosuria broken only by short intermissions, the islands of Langerhans showed no alterations.

Fatal intraperitoneal doses of adrenalin may set up an acute hemorrhagic pancreatitis in which some of the islands of Langerhans, together with other structures, suffer alteration; but control experiments with intravenous injections indicate that the lesions observed are not necessary to the production of glycosuria.

On Certain Relations between the Adrenal Glands and Carbohydrate Metabolism. The knowledge that extracts of the adrenal gland have the property of inducing glycosuria suggested the inquiry whether the adrenal glands normally possess any influence on carbohydrate metabolism by virtue of their internal secretion. Experiments showed that compression of the adrenal glands is followed by glycosuria; while their exclusion, by extirpation or ligation of their vessels, is followed by a considerable fall in the sugar-content of the blood. These results were confidently interpreted as indicating that the adrenal glands stand in an important relation to carbohydrate metabolism and normally exert a regulatory influence upon the sugar-content of the blood.[1] Unforeseen experimental difficulties have up to the present time made it impossible to prove whether the influence of the adrenals on carbohydrate metabolism is of the nature suggested in the hypothesis that was proposed—that is to say, an influence exerted through the internal secretion of the gland. It is not without interest

[1] Medical News, October 25, 1902.

to review briefly the main facts that have come to light in the course of this study.

On subjecting the adrenal glands of normal dogs (fed on lean meat) to intermittent compression between the thumb and finger glucose quickly appears in the urine. The percentage of sugar may be high (4 or 5 per cent.), but the amount has never been large, and the duration of the glycosuria is not more than a few hours. It is not necessary in order to obtain these results to compress the gland to the point where its structures yield sensibly to the fingers. Control observations on the spleen, in which the organ was much damaged by pressure, failed to show glycosuria. Destructive compression of the pancreas may be followed by the appearance of a small amount of sugar in the urine.

These results were at first interpreted to indicate that the process of compression leads to glycosuria by causing a substance allied to the glycosuria-producing substance of adrenal extracts to enter the blood. It now appears uncertain whether this is the real explanation. In animals the carotids of which were connected with a mercury manometer the adrenal glands were intermittently compressed without giving rise to any increase in the general blood pressure such as one might perhaps expect if the internal secretion of the gland were actually being forced into the circulation in unusual amount. This observation, together with the fact that compression of the pancreas may occasion glycosuria, makes it necessary to admit that nervous influences may be largely responsible for the sugar which appears after compressing the adrenals. Nevertheless, the fact that compression of a single adrenal gland may occasion pronounced glycosuria suggests that functional disturbances in this gland readily bring on at least a temporary glycosuria.

Numerous experiments have been made in which the adrenal vessels were either ligatured or in which the adrenal glands were extirpated bilaterally. In most of these observations the blood sugar-content before operation was compared with the blood sugar-content about four hours after operation. A considerable fall in the percentage of blood sugar was found in almost all instances. Controls show that this fall cannot be accounted for either by the slight lengthening of the fasting period or by the small amount of blood (8 to 25 grammes) abstracted for the determination of the blood sugar.

In a few instances the blood sugar after operation on the adrenals has been somewhat increased after the lapse of four hours. There is good reason to think that etherization usually increases somewhat the sugar-content of the blood, and it is likely that our exceptional results can be accounted for by the action of this anæsthetic. The fact that we do not know any narcotic or anæsthetic which does not in itself affect the sugar-content of the blood is still an obstacle to the correct

TABLE ILLUSTRATING THE FAILURE OF ADRENALIN TO INDUCE GLYCOSURIA.

Weight of dog.	Nature of diet, etc.	Nature of operation on adrenals.	Interval between operation and injection of adrenalin.	Dose of adrenalin.	Mode of administration.	Catheterization following adrenalin after	Volume of urine.	Sugar.	Remarks.
6.9 kilo.	Lean meat.	Adrenal vessels ligatured.	3 h. 25 min.	5 c. c. (1–1000)	Intraperitoneal	1 hour. 2 hours. 3 " 4 "	5 c. c. 4 " 8 " 13 "	Trace. Negative. Trace. Negative.	A second injection of 9 c.c. adrenalin (1–1000) on following day, quite negative as regards sugar.
6.8 kilo.	Unknown; well nourished; lacteals full.	Adrenal vessels ligatured.	4 h. 40 min.	5 c. c.	Intraperitoneal	1 hour. 2 hours. 3½ "	5 c. c. 4 " 12 "	Negative. " "	No fluid in peritoneal cavity.
9.1 kilo.	Lean meat.	Right adrenal vessels tied; left gland removed.	4 h. 15 min.	7.5 c.c.	Intraperitoneal	1 hour. 2 hours. 3½ "	10 c. c. 4 " 9 "	Negative. " "	No fluid in peritoneal cavity.
8.7 kilo.	Lean meat, starved 60 hours.	Adrenal vessels ligatured.	4 h. 35 min.	8 c. c.	Intraperitoneal	36 min.	4 c. c.	Trace.	A subsequent injection of one sheep's gland (dried) caused the appearance of 0.5–1 per cent. reducing substance in 200 c.c. urine.
15.6 kilo.	Starved 40 hours; well nourished.	Adrenal vessels ligatured.	4 h. 20 min.	8 c. c.	Intraperitoneal	1 hour. 2 hours. 4 " 17 "	5 c. c. 12 " 40 "	Negative. Trace. Slight trace. Negative.	No fluid in peritoneal cavity.
7.7 kilo.	Starved 40 hours; fairly well nourished.	Adrenals removed.	4 hours.	5 c. c.	Intraperitoneal	1 hour. 4 hours.	3 c. c. 5 "	Slight trace. " "	No fluid in peritoneal cavity.
8.2 kilo.	Unknown; well nourished.	Adrenals removed.	3 h. 50 min.	4 c. c.	Intraperitoneal	1 hour.	3 c. c.	Negative.	
15.9 kilo.	Starved 40 hours; well nourished.	Adrenals removed.	5 hours.	8 c. c.	Intraperitoneal	1 hour. 3 hours.	10 c. c. 35 "	Negative. "	

interpretation of our results. Whether the fall in blood sugar which we have noted after the above-mentioned operations on the adrenals can be attributed wholly or in part to the exclusion of the internal secretion of these glands is not yet clear.

It is a fact of considerable interest that under certain conditions the injection of adrenalin into the peritoneal cavity failed to bring on glycosuria after the adrenal vessels had been ligatured or the adrenal glands had been extirpated. This result is the more striking because of the great regularity with which intraperitoneal injections of adrenalin induce marked glycosuria in normal dogs. If the injection of adrenalin be made within two hours of the operation on the adrenal glands glycosuria usually appears, but in every instance where the injection was not given until the lapse of four hours or a longer period sugar either did not appear in the urine or appeared in mere traces. The table on page 57 makes this point clear.

The necessity for control observations is, of course, obvious, and the following experiments are of interest in this connection:

Experiment 1. Dog; weight, 7 kilos. Poorly nourished; not fed for twenty-four hours. The mesenteric vessels passing to and from a loop of jejunum six inches in length were ligated with two ligatures, and the loop itself was tied off. No ether used. Four hours after this operation 4 c.c. adrenalin chloride solution (1 : 1000) were injected into the peritoneal cavity; 8 c.c. of urine collected one hour later showed 6.2 per cent. sugar.

Experiment 2. Dog; weight, 18 kilos. Well nourished; twenty-four hours' fast. Etherized and vessels and nerves of the spleen ligatured about one and a half inches from the spleen, numerous ligatures being employed. First hour after operation 35 c.c. urine, about 0.5 per cent. sugar; second hour after operation 10 c.c. urine, about 0.3 per cent. sugar; third hour after operation 11 c.c. urine, slight reduction; fourth hour after operation 13 c.c. urine, negative or slight trace. After four hours animal received 8 c.c. adrenalin chloride solution (1 : 1000) in the peritoneal cavity. Fifty-five minutes later 49 c.c. urine, 2.8 per cent. sugar; two hours and a half later 40 c.c. urine, 6.1 per cent. sugar.

Experiment 3. Dog; weight, 11 kilos. Well nourished; not fed for twenty-four hours. Etherized and splenic vessels and nerves tied off with numerous ligatures, as in Experiment 2. First hour after operation 14 c.c. urine gave 0.44 per cent. sugar; second hour after operation 14 c.c. urine gave a slight reduction; third hour after operation 18 c.c. urine gave a slight reduction; four and a quarter hours after operation 18 c.c. urine gave a trace of reduction. After four and a quarter hours animal received 5 c.c. adrenalin in the peritoneal cavity. Fifty minutes later 23 c.c. urine gave 1.78 per cent. sugar; two and a half hours later 35 c.c. urine gave 4.9 per cent. sugar.

These and similar control experiments show that operations on the spleen or intestine do not lead to an abolition of the property of adre-

nalin to induce glycosuria when put into the peritoneal cavity. It occurs to one that the operation of ligating the adrenal vessels or extirpating the glands may be followed by a disturbance of absorption from the peritoneum; but if this be the case it is difficult to see why it should not also follow operations on the spleen. It also occurs to one that the injected adrenalin may have been mixed with blood, and thus rendered less active; but hemorrhage did not occur in any case, and the peritoneal cavity was in several instances practically free from fluid. The failure of adrenalin to cause glycosuria in our experiments seems to point to some special influence connected with the exclusion of the adrenals; but whether the real explanation lies in the elimination of the adrenal internal secretion, or in some obscure nervous disturbance, it has not been possible to determine. It is not certain that the adrenalin used in these experiments is equivalent to the internal secretion of the dog's adrenals.

In five dogs from which the pancreas was totally removed after bilateral ligation of the adrenal vessels it was observed that the urine subsequently passed either contained no sugar or only a small quantity.

In those cases where the urine contained some sugar this disappeared before the lapse of many hours. Comparing these results with those which we have obtained from numerous extirpations of the pancreas alone, there seems to be no doubt that exclusion of the adrenal glands modifies the onset of pancreatic glycosuria in the direction of greatly reducing the early excretion of sugar.[1] Even in cases where the

[1] Experiments 1, 2, and 3 illustrate the inhibition of pancreatic glycosuria after operations on the suprarenals. A similar inhibition was not observed after ligature of splenic vessels. Controls involving operations on the nervous system only have not been made.

Experiment 1. Dog; weight, 10 kilos. Bladder emptied; urine normal. Suprarenal vessels ligatured on both sides. Immediately afterward pancreas completely extirpated.

One hour 15 minutes after pancreatic extirpation, 2¾ c.c. urine contained no sugar.

Two hours 30 minutes after operation, 6 c.c. urine contained about 0.3 per cent. sugar.

Three hours 30 minutes after operation, 12 c.c. urine with 10 c.c. Fehling's solution gave slight greenish reduction.

Four hours 30 minutes after operation, 8 c.c. urine, negative for sugar.

Experiment 2. Dog; weight, 10.9 kilos. Bladder emptied; urine normal. Suprarenal vessels ligatured on both sides; 27 minutes later pancreas had been completely extirpated.

One hour after operation, 5 c.c. urine contained about 0.5 per cent. sugar.

Two hours after operation, 4 c.c. urine contained about 0.4–0.5 per cent. sugar.

Three hours after operation, 1.5 c.c. urine contained 0.3–0.4 per cent. sugar.

Four hours thirty minutes after operation, 4–5 c.c. bloody urine contained no sugar.

Experiment 3. Dog; weight, 9.1 kilos. Bladder emptied, urine normal. Suprarenal vessels ligatured on both sides. Twenty-five minutes after completion of these operations the pancreas had been completely extirpated.

One hour 45 minutes after last operation, 6 c.c. urine contained not more than 0.2 per cent. sugar.

Three hours 45 minutes after last operation, 9 c.c. urine gave very slight reduction.

Five hours 45 minutes after last operation, 10 c.c. urine, quite negative.

Ten hours after last operation, 9 c.c. urine, quite negative.

Experiment 4. Dog; weight, 9.2 kilos. Bladder emptied, urine normal, pancreas completely extirpated. One hour later 10 c.c. urine contained 7 per cent. sugar. One hour and

adrenal operation follows extirpation of the pancreas a high grade of glycosuria may be rapidly lessened; but ultimately the excretion of sugar again reaches a high level, so that the adrenal influence, whatever it may be, is a transient one. In the interpretation of these results one has to bear in mind that the glycosuria of simple pancreatic extirpation may show for a time a spontaneous falling off in the quantity of sugar excreted. It seems to us probable that a severe form of shock may be responsible for the inhibition of pancreatic glycosuria that has been observed.

Although the experimental results that have been here described point to a closer relationship between the adrenal glands and carbo-

15 minutes after pancreatic extirpation right adrenal vessels were tied; 8 minutes later left adrenal vessels were tied. Urine collected 12 minutes later contained 6.5 per cent. sugar.

One hour after ligation of adrenals, 6 c.c. urine contained 5.6 per cent. sugar.

Four hours after ligation, 20 c.c. urine contained 4.6 per cent. sugar.

Eight hours after ligation, 20 c.c. urine contained 0.6 per cent. sugar.

Soon after suppression of urine occurred.

Experiment 5. Dog; weight, 16.8 kilos. Bladder emptied, urine normal, pancreas completely extirpated. Twenty minutes later right adrenal vessels tied. Urine obtained by catheter showed slight reduction. One hour after operation on left adrenal, 5 c.c. urine contained 6.7 per cent. sugar. Ten minutes later left adrenal vessels tied.

1 hour 15 minutes after ligation of left adrenal vessels, 13 c.c. urine contained 4.5 p. c. sugar.

2 hours 15 minutes	"	"	"	17 c.c.	"	1.6	"	"
3 hours 15 minutes	"	"	"	40 c.c.	"	0.2	"	"
4 hours 15 minutes	"	"	"	16 c.c.	"	0.3	"	"
5 hours 15 minutes	"	"	"	27 c.c.	"	1.25	"	"
6 hours 15 minutes	"	"	"	13 c.c.	"	1.75	"	"
7 hours 15 minutes	"	"	"	4.5 c.c.	"	2.25	"	"
8 hours 15 minutes	"	"	"	8 c.c.	"	2.25	"	"

Soon after this suppression set in.

Experiment 6. Dog; weight, 8.7 kilos; starved 60 hours. Bladder emptied, urine normal, pancreas completely extirpated. Urine immediately after contained no sugar. Twenty-seven minutes after extirpation adrenal vessels tied on both sides. Urine immediately after contained no sugar.

1 hour after ligation of adrenal vessels, 6 c.c. urine contained 0.1–0.2 per cent. sugar.

3 hours	"	"	5 c.c.	"	a trace of sugar.			
4 hours	"	"		"	"	"		
9 hours	"	"	34 c.c.	"	"	"		
23 hours	"	"	12 c.c.	"	2.2 per cent. sugar.			
28 hours	"	"	5 c.c.	"	5.0	"	"	
29 hours	"	"	10 c.c.	"	5.5	"	"	
32 hours	"	"	17 c.c.	"	5.0	"	"	

Experiment 7. Dog; weight, 7.7 kilos; not fed for 30 hours before operation. Bladder emptied, urine normal; pancreas totally extirpated at 4.05 P.M.; aseptic operation.

2 hours after operation, 4 c.c. urine contained 7 per cent. sugar.							
5 hours	"	45 c.c.	"	8	"	"	
19 hours	"	140 c.c.	"	9	"	"	
23 hours	"	35 c.c.	"	14.3	"	"	

On the following day, 23 hours after the pancreatic extirpation, the adrenal vessels were ligated on both sides.

1 hour after ligating adrenal vessels, 11 c.c. urine contained 6.25 per cent. sugar.

2 hours	"	"	13 c.c.	"	6.5	"	"
3 hours	"	"	13 c.c.	"	6.5	"	"
7 hours	"	"	26 c.c.	"	5	"	"

Subsequent collections were impracticable, although the animal lived nearly 24 hours longer.

hydrate metabolism than has been previously recognized, it cannot be maintained that we have as yet succeeded in obtaining unequivocal evidence that the phenomena described are due to the excessive influence of the adrenal internal secretion or to the exclusion of this secretion from the circulation. Some of these phenomena can probably be equally well accounted for on the supposition that imperfectly understood nervous factors have been brought into play. It must, therefore, be left to further experiments, in which close attention is given to control observations on the nervous system, to determine whether the internal secretion hypothesis is tenable.

A REPORT OF TWO CASES OF MULTIPLE SCLEROSIS, WITH NECROPSY:

WITH REMARKS ON MUSCULAR ATROPHY, SECONDARY DEGENERATION, AND LOSS OF TENDON REFLEXES, WITH INCREASED MUSCULAR TONICITY, OCCURRING IN THIS DISEASE.[1]

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(From the William Pepper Clinical Laboratory, Phoebe A. Hearst Foundation.)

Multiple sclerosis seems to be a rare disease in America, and scarcely any cases with necropsy are to be found in the literature of this country. I am inclined to think that some cases are overlooked, and that the disease, while uncommon, does occur more frequently than the paucity of records gives us reasons to believe. B. Sachs remarked at the time he wrote his critical digest on multiple sclerosis, in 1898, that he had been able to find only one necropsy record of a case of this disease published in America, and that was by Seguin, and was incomplete.

Since the publication of Sachs'[2] paper a case with necropsy has been reported by Burr and McCarthy[3] (1900), and another that probably should be classed under multiple sclerosis, although published only in abstract, May, 1902, by J. R. Hunt.[4] The paper by E. W. Taylor[5] is one of the best on the subject by American writers, but the cases he reports occurred in Germany, and are a contribution to German literature.

I report two cases, with microscopic examination of the nervous tissues. The first case was in the service of Dr. F. X. Dercum, at the

[1] Read in abstract at the annual meeting of the American Neurological Association, June 1902.

[2] Sachs. Journal of Nervous and Mental Disease, 1898.

[3] Burr and McCarthy. Ibid., 1900.

[4] J. R. Hunt. Ibid., May 12, 1902, p. 288.

[5] E. W. Taylor. Deutsche Zeitschrift für Nervenheilkunde, vol. v.

Philadelphia Hospital, and is a typical example of the disease. I am indebted to Dr. Dercum for the clinical history and the pathological material. The second case was in my service at the Philadelphia Hospital, and forms a striking contrast in its clinical aspects to Dr. Dercum's case.

CASE I.—C. O., laborer, white, aged twenty-five years, was admitted to the Philadelphia Hospital, March 26, 1900. A brief history was taken at this time.

November 6, 1900. Chief complaint: stiffness and weakness of right upper and lower limbs, vertigo, and tremor.

Father died, at the age of fifty years, from gastric disease; mother died after labor; one brother died in infancy. Three sisters and four brothers are living and well.

The patient had measles when a child and typhoid fever seven years ago. He has used alcohol and tobacco to excess, but denies venereal disease.

Two years ago last winter he worked four or five hours one night in the hold of a vessel with nothing on but trousers, drawers, shoes, and stockings. Thus clad he came up on the deck, when it was bitterly cold and raining sleet and hail, and took a drink of ice-water. He remained on deck about twenty minutes, not noticing the cold, and then returned to the hold, where he worked for six hours more. In the morning he went home and to bed, still experiencing no ill effects from the exposure. That afternoon he felt stiff all over, and the stiffness remained for several days. Four days after this exposure he had to work seven hours in the hold of a ship shovelling wet coal. While shovelling he stood in the wet coal, and afterward had to sit in the wet, shivering, while waiting for more coal. The next morning he went directly from the hold to the deck, to sweep. As soon as he reached the deck he began to feel stiff, and staggered and was hardly able to walk. That night he experienced sharp pains in the thighs, more in the right thigh, and the stiffness was most marked on the right side.

This condition remained stationary for one month, when he awakened one morning with sharp pains in the right leg, with marked rigidity of that member. Soon after this he suffered from similar pains in the left leg, although not so severely.

His condition improved slightly for several months following, but there has been little change during the past year. He has occasionally had loss of sphincter control during the past year.

Present Condition (*November* 6, 1900). The patient is a well-developed young man. His intelligence is not impaired, but his speech is slow and scanning. Pupils are equal and the irides respond promptly to light and in accommodation. The ocular muscles are apparently normal. There is a slight tremor of the tongue. The tendon reflexes of the upper limbs are normal (later those of the right upper limb were exaggerated). The epigastric reflex is normal, but the abdominal and cremasteric reflexes are absent. The patellar reflex is exaggerated on each side, more so on the right side. Ankle clonus is present on each side. Babinski's reflex is present. Grip of the right hand by dynamometer is 41; of left, 45. He has apparently very little loss of power in the upper or lower limbs. Temperature sense is normal,

except in the feet, where there is delayed sensation, and in the toes and heel of the right foot, where there is reversal of temperature sense. Tactile and pain senses are unimpaired. Station is poor. He sways with his eyes open and falls when they are closed. Gait is staggering and the right foot is dragged. Some ataxia is observed in the upper limbs, especially on the right side. Intention tremor is present in the right upper limb.

The report of the examination of the eyes by Dr. G. E. de Schweinitz, November 18, 1900, is as follows: "Light reflex normal. Each disk atrophic; atrophy more marked on temporal side. No change in vessels except a slight perivasculitis. Well-marked nystagmus."

December 8, 1901. He has wasted very rapidly during the past two months, and during the past month has had almost absolute loss of power in his lower limbs, especially on the right side. The wasting is general. Breath smells sweetish, and examination of urine shows sugar in large amount.

The patient died December 9, 1901.

The microscopic examination of the brain and spinal cord, made by me, revealed numerous areas of sclerosis, especially in the cord. It is not necessary to dwell on the pathological condition, as it was like that commonly seen in multiple sclerosis. The case was clinically and pathologically a typical one of this disease. I had the opportunity to examine this patient frequently during his residence in the hospital.

The causative relation of cold and dampness to multiple sclerosis seems to be clearly shown in this case. Krafft-Ebing has insisted on this etiology of the disease, but it is seldom that the symptoms follow so closely the exposure, as in this case. The man C. O. developed the symptoms of multiple sclerosis after repeated and long exposure to cold and dampness in shovelling coal in the hold of a vessel. Residence in a damp house was believed to be the cause of the disease in the second case. It is probable that this was not the only cause in either case.

Case II.—The patient, a woman aged fifty-one years, was in my service at the Philadelphia Hospital during the summer of 1901. She said the first symptoms of her disease began in 1891 or 1892 after a residence in a damp house. She denied venereal disease and abuse of alcohol, although she acknowledged that she had used much tobacco. Impaired gait was noticed early, but the gait soon improved, and later became worse again. She was able to walk until 1899, but staggered so that she had to be supported. In 1891, while doing housework, she suddenly became numb in the feet, and the numbness extended gradually up the limbs, with progressive loss of power. In two days the numbness had extended to the waist, and she had a girdle sensation of pressure and incontinence of urine and feces. Her speech was slow, and she had some difficulty in saying words. My notes, made June 24, 1901, are as follows:

The lower limbs appear to be completely paralyzed, and although they are drawn up at times, the movement is probably entirely involuntary. When told to move her toes she is unable to do so. The lower limbs are wasted. The right thigh in its middle portion measures

thirteen inches; the left thigh in the corresponding portion measures fourteen inches. The thighs are proportionately more atrophied than the legs below the knees, but the atrophy in the latter is partly masked by œdema. The feet are very œdematous and pit on pressure. Pressure over either leg causes the leg to be drawn up; this is especially true of the left lower limb. The movement is the result entirely of reflex action, and is involuntary. The knees and feet are inverted, and there is much spasticity of the lower limbs, which is greatly increased by passive movement. *There is no knee-jerk on either side, even with reinforcement.* This is especially noteworthy because of the spasticity in the lower limbs. The knee-jerk is not prevented by the spasticity, as the spasticity is comparatively slight when the limbs have not been irritated, and even without irritation of the limbs there is no knee-jerk. When the attempt is made to obtain the knee-jerk there is no contraction visible in the quadriceps muscle of either side. Ankle clonus is not obtained on either side. The Babinski reflex is very pronounced on each side, the great toe as well as the other toes being drawn forcibly upward. The Achilles jerk is absent on each side. Sensation for touch, pain, and temperature is normal in the lower limbs. No tenderness is produced by pressure of the nerves or muscles.

The movements in the upper limbs are free, and the resistance to passive movements in these limbs is proportional to the muscular development. The upper limbs above the elbow are fairly well developed. The interossei muscles, the thenar and hypothenar eminences are much wasted, and the grasp of each hand is almost *nil.* The forearms are wasted, but not intensely so. Sensation for touch, pain, and temperature is normal in the upper extremities and over the chest. The tendon reflexes of the upper limbs, biceps tendon, triceps tendon, and wrist-jerks on either side are not strikingly abnormal. No tenderness is felt on pressure of nerves or muscles.

The cranial nerves are not distinctly implicated. The tongue is protruded straight. The masseters contract firmly. The corner of the mouth is drawn up well on each side, and the eyes are firmly closed. At the present examination there is considerable swelling of the left eyelid.

The spinal column is normal.

The mentality is feeble. The patient replies correctly to questions, but her statements concerning her past condition are not fully reliable. She complains of numbness in her hands. She has incontinence of urine and feces.

The report of the examination of her eyes, made by Dr. H. F. Hansell, June 24, 1901, is as follows:

"Paralysis of the third nerve of the right side and also of the left, amounting to almost complete ophthalmoplegia. Pupillary response is good. Pupils are equal. Partial atrophic cupping of both optic nerves, with reduction in size of the bloodvessels, without signs of previous inflammation."

The patient grew gradually worse, and died July 5, 1901.

The microscopic examination, made by me, gives the following results:

Numerous sclerotic areas are found throughout the brain and spinal cord. One such area is found implicating the nuclei of the oculomotor, trochlear, and abducent nerves, but is not confined to these nuclei. The nerve cell-bodies of the oculomotor nuclei are not very distinctly diseased, as shown by the thionin stain, and yet some may be slightly altered. The posterior longitudinal bundle on each side is in the sclerotic area, and contains at this part a few medullated nerve fibres. Half of the medulla oblongata at one level has undergone a sclerotic change. A sclerotic area is found in the left optic nerve, but the right optic nerve appears to be normal.

Some degeneration, as shown by the Marchi method, is detected in the sclerotic areas of the spinal cord. Secondary degeneration of moderate intensity is found in each crossed pyramidal tract, below the

FIG. 1.

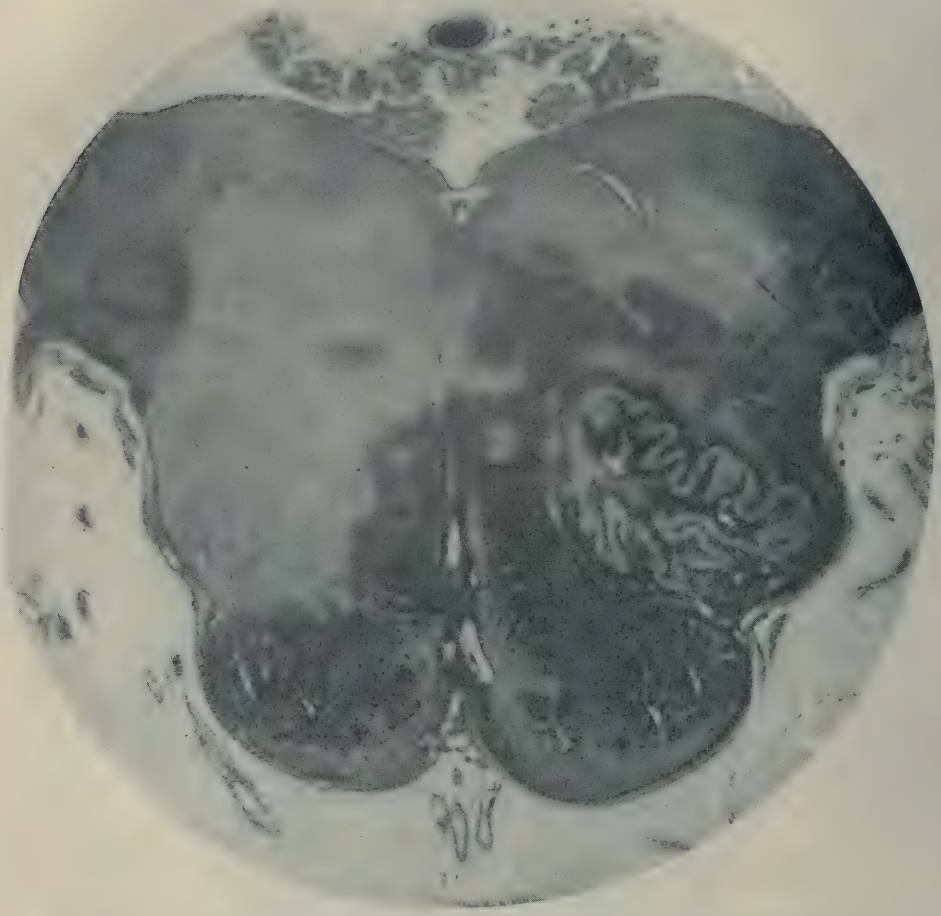


CASE II.—Section through the nuclei of the oculomotor nerves, showing a sclerotic patch implicating these nuclei.

mid-thoracic region, but is greater on one side. No sclerotic areas are found in the posterior columns at the upper lumbar region, but in the mid-lumbar region a sclerotic area is present on each side of the posterior septum, and implicates the posterior root fibres after their entrance into the posterior columns. These areas do not extend into the lower lumbar region, but here a sclerotic area is found implicating one anterior horn and the antero-lateral column. A sclerotic area implicates the greater part of the left anterior and lateral columns and the gray matter of the left side and a part of the left posterior columns in the sacral region. A sclerotic area is found also in the right lateral column, and gray matter of the right side in the sacral region. Many of the nerve cell-bodies of the anterior horns of the cervical and lumbar region appear shrunken and have imperfect dendritic processes, and some are much pigmented. The thionin stain was employed. The

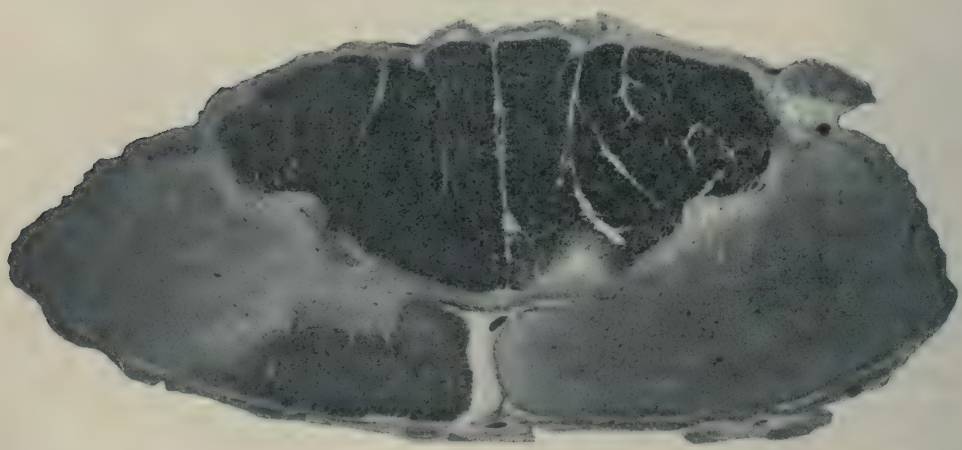
nerve cell-bodies in a sclerotic area implicating one anterior horn in the lower lumbar region resemble very closely those of the other horn

FIG. 2.



CASE II.—A sclerotic area implicates a large portion of the medulla oblongata.

FIG. 3.



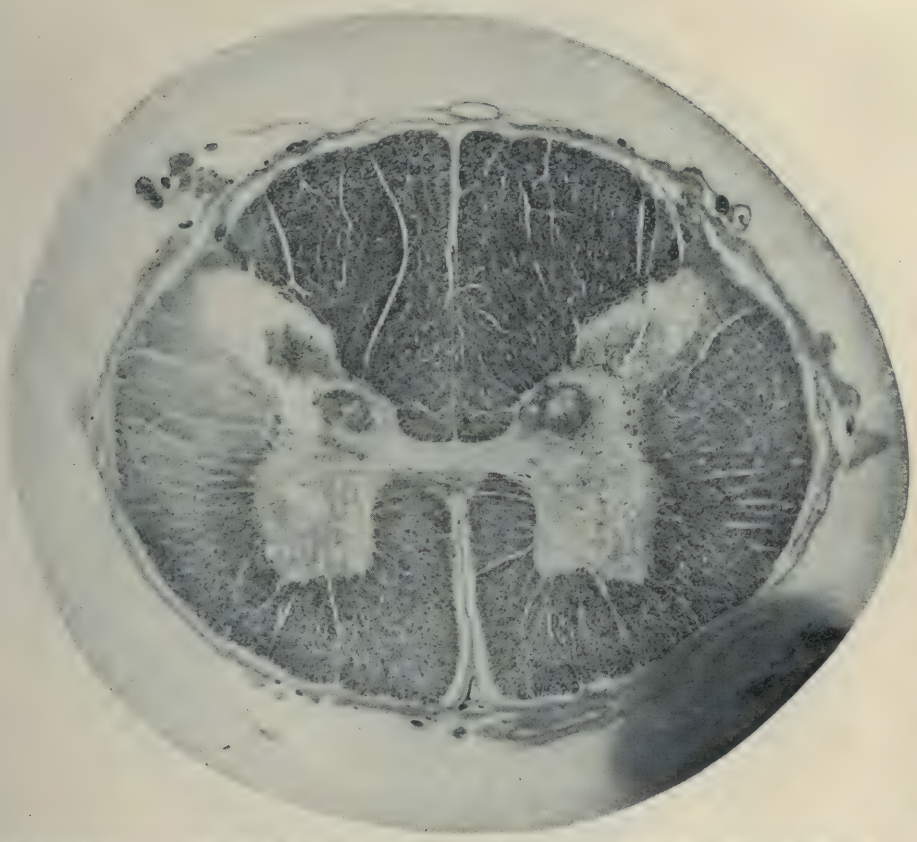
CASE II.—Section from the cervical region, showing a large sclerotic patch on each side of the spinal cord.

in the same section where there is no sclerotic area, and in neither horn are they normal. A branch of one of the plantar nerves is partially degenerated. Many other sclerotic areas not described are found in the brain and spinal cord.

A summary of the case is as follows:

In 1891 the patient—a woman, then about forty-one years of age—complained of numbness in the feet, and soon the legs became numb. She had at this time progressive loss of power in the lower limbs and

FIG. 4.

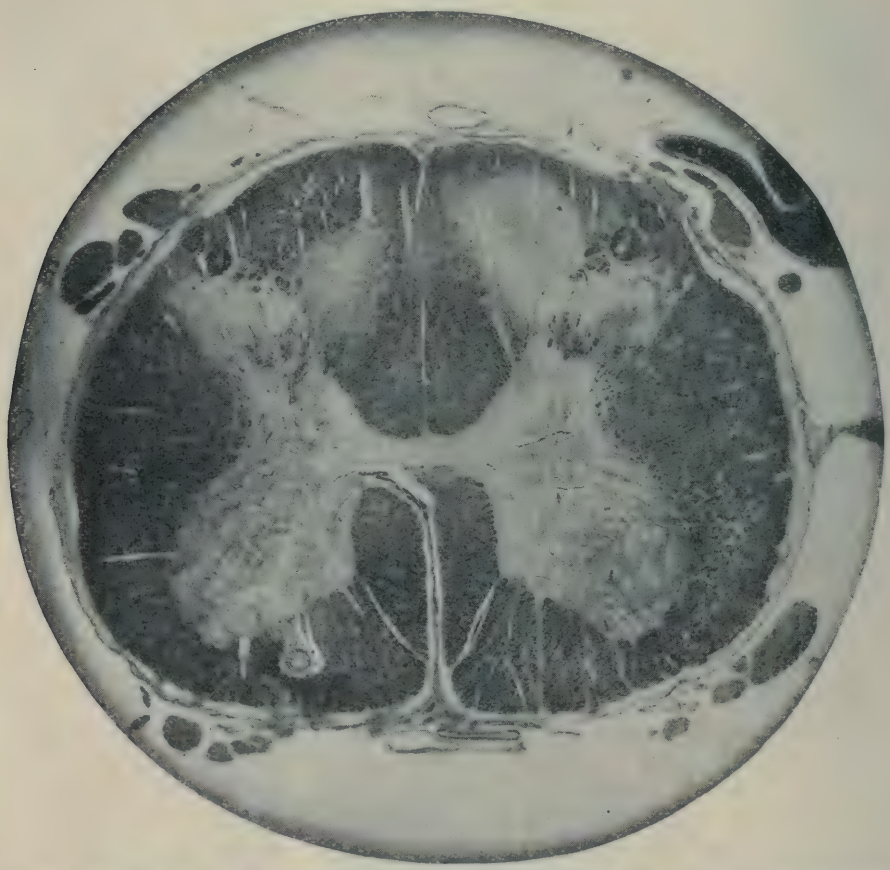


CASE II.—No sclerotic area is seen in the posterior columns in this section from the upper lumbar region. The secondary degeneration of the crossed pyramidal tracts is not well reproduced in the photographs.

staggering gait. Within two days the numbness extended as high as the waist, and she complained of girdle sensation, and had complete paralysis of the lower limbs. She had also incontinence of urine and feces. She had resided in a damp house. The disturbance of gait soon disappeared for a time, and she was able to walk with difficulty until 1899, but staggered. She complained of shooting pains at times in the knees, extending to the ankles. In 1901 her speech was somewhat drawling. The lower limbs were completely paralyzed, were much wasted, and spastic; slight irritation causing the limbs to be drawn up involuntarily, and yet the patellar and Achilles reflexes

were absent. The knees and feet were inverted. The Babinski reflex was very pronounced. Sensation was normal everywhere. Voluntary movement in the upper limbs was impaired, and the grasp of the hands was very feeble. The hands were very much atrophied. The tendon reflexes of the upper limbs were normal. Mentality was feeble. She had almost complete external ophthalmoplegia and partial atrophic cupping of both optic nerves. Iritic response was good. The case was one of disseminated sclerosis, as shown by the microscopic examination.

FIG. 5.



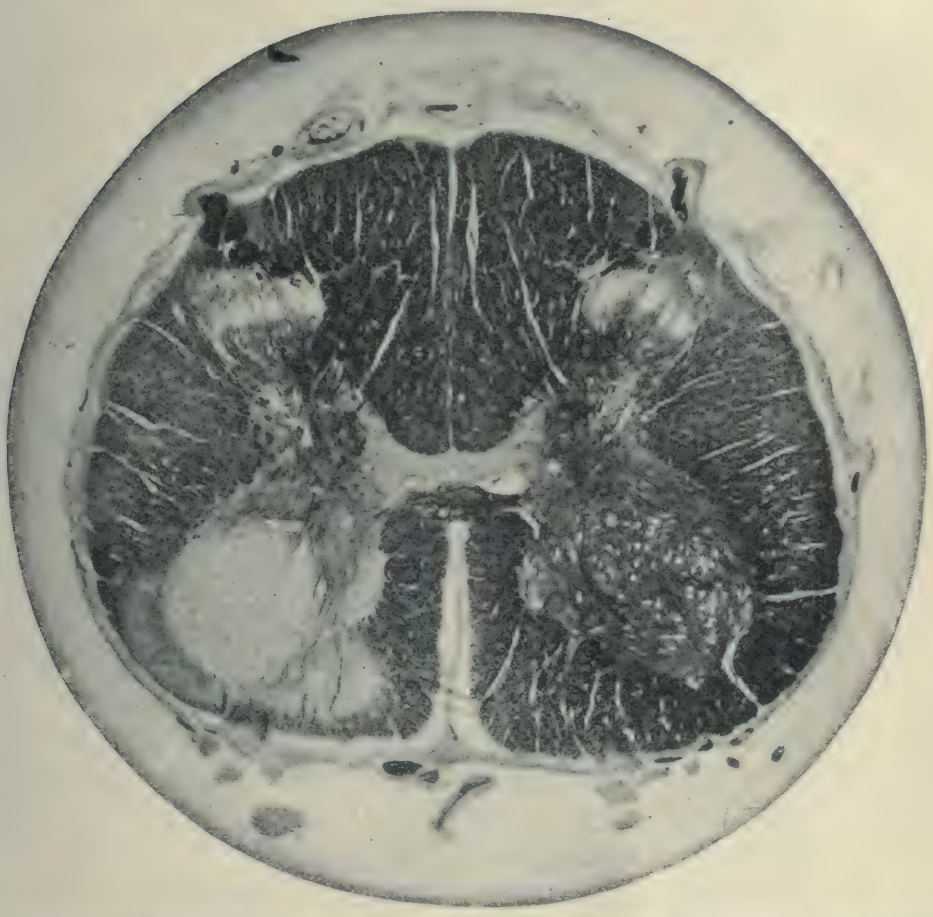
CASE II.—Section from the mid-lumbar region. A sclerotic area is seen on each side of the posterior septum only in the mid-lumbar region (compare Fig. 5 with Figs. 4 and 6). The tendency to symmetry of the areas in multiple sclerosis is well shown in this section.

The interesting features of this case were: The pronounced muscular atrophy; the secondary degeneration of the crossed, pyramidal tracts, more distinct, however, on one side, in a case of disseminated sclerosis; the loss of the patellar and Achilles reflexes, with spasticity of the lower limbs, the loss of these reflexes probably being the result of sclerotic areas in the posterior columns and a part of the anterior horns of the lumbar and sacral regions; and the almost complete external ophthalmoplegia resulting from a sclerotic area in the nuclei of the third, fourth, and sixth nerves.

The muscular atrophy was very pronounced in the lower and upper limbs, and in the latter the atrophy was more distinct in the small muscles of the hands. The atrophy in the lower limbs below the knees was partly masked by œdema. Oppenheim[1] regards muscular atrophy as a rare sign of multiple sclerosis, and states that, as a rule, the muscles preserve their normal size and electrical reactions.

L. Brauer[2] believes that muscular atrophy is very uncommon in the early stages of multiple sclerosis, and he reports a case of this disease

FIG. 6.



CASE II.—Section from the lower lumbar region. The sclerotic areas of the posterior columns represented in Fig. 5 have disappeared, but a sclerotic area is seen in one anterior horn extending into the white matter.

in which muscular atrophy was an early symptom and later became very pronounced. He acknowledges that muscular atrophy does occur occasionally in multiple sclerosis, and he believes it affects especially the small muscles of the hand and the peroneus distribution. He refers to cases of muscular atrophy occurring in multiple sclerosis reported

[1] Oppenheim. Lehrbuch der Nervenkrankheiten, third edition, p. 314.
[2] Brauer. Neurologisches Centralblatt, July 15, 1898, No. 14, p. 635.

by Jolly, Ebstein, Leube, Schüle, Buchwald, Otto, Engesser, Dejerine, and Pitres. Killion also is said to have observed muscular atrophy in multiple sclerosis.

Probst[1] speaks of the infrequency of muscular atrophy in multiple sclerosis, and refers to a few cases in which it was observed. In most of these cases no very important alteration of the cell-bodies of the anterior horns was seen, but Probst was able to find a decrease in the number and a shrinkage of the cell-bodies in the anterior horns of the upper cervical region in one case of multiple sclerosis with muscular atrophy, although no sclerotic focus could be found in this region. This case Probst pronounces as unquestionably one of multiple sclerosis. Alteration of the nerve cell-bodies was observed by me in my case. According to Probst, alteration of nerve cell-bodies in multiple sclerosis has been observed by Bourneville, Guérard, Charcot, Fromann, Gowers, Obersteiner, Frommann, Taylor, Schuster, and Bielschowsky; but muscular atrophy does not appear to have been observed in all these cases in which cellular change existed.

Secondary degeneration is not seen in multiple sclerosis, according to some writers, and yet in my case it could be found in the crossed pyramidal tracts in the spinal cord below the mid-thoracic region. According to Probst,[2] Schultze was the first to offer as an explanation of the absence of secondary degeneration the preservation of the axons in the sclerotic foci. Secondary degeneration in multiple sclerosis is said to have been observed by Jolly in 1872, Buss in 1889, Werdnig in 1888, Babinski in 1885, Redlich in 1895, and Rossolimo— certainly a small number of cases, in consideration of the large number of cases of this disease published. In most of the cases in which secondary degeneration was found it extended only a short distance, and was only of moderate degree. In a case reported by Probst[3] secondary degeneration of the anterior and lateral pyramidal tracts existed, and extended from the proximal portion of the pons into the lumbar region. Probst mentions that possibly some might regard his case as one in which multiple sclerosis was combined with amyotrophic lateral sclerosis, inasmuch as the nerve cell-bodies of the anterior horns were not normal and sclerotic foci were not found in the spinal cord. This combination, I think, might occur, as both diseases possibly are the result of faulty development of nervous tissue in the embryo.

Since my paper was read before the American Neurological Association an interesting article in which the occurrence of secondary degeneration in multiple sclerosis is considered has been published by Schupfer.[4] He says secondary degeneration in this disease has been observed only

[1] Probst. Deutsche Zeitschrift für Nervenheilkunde, 1898, vol. xii.
[2] Loc. cit.
[3] Loc. cit.
[4] Schupfer. Monatsschrift für Psychiatrie und Neurologie, August, 1902, p. 109.

by Jolly, Westphal, Schultze, Greiff, Babinski, Werdnig, Buss, Rossolimo, Probst, Thomas and Long, and Taylor. He subjects these cases to a critical study, and concludes that only in the cases of Buss, Probst, and Thomas and Long was the degeneration of the pyramidal tracts in connection with lesions in the spinal cord, medulla oblongata, and pons. In Thomas and Long's case the cause of the degeneration he thinks was syphilitic endarteritis. Degeneration of the pyramidal tracts is therefore, in his opinion, extremely rare in multiple sclerosis, and may be caused by sclerotic foci or may occur independently of these. The secondary degeneration of the pyramidal tracts may be associated with diffuse sclerosis of the cerebral hemispheres with atrophy of the gyri and alteration of the cells of the central gyri, as in the cases of Schultze and Greiff. The occurrence of degeneration of the pyramidal tracts without focal lesions he finds difficult to explain. It is possible that Schupfer does not lay sufficient importance upon the short extent of some of the foci in multiple sclerosis, and important areas of sclerosis of limited extent may be overlooked. In Jolly's case and Schultze's, Schupfer says the sclerotic areas do not explain the degeneration of the pyramidal tracts, as the degeneration began at a part where sclerotic areas were not detected. It is important to bear in mind the cumulative effect of slight degeneration at different levels; this, however, Schupfer does not overlook.

The loss of the patellar reflexes, with increase in the muscular tonicity of the lower limbs, was noteworthy. There could be no mistake in regard to this, because in my notes made at the time of the clinical examination I underscored twice the statement bearing on this point. The statement reads: "The knees and feet are inverted, and there is much spasticity of the lower limbs, which is greatly increased by passive movement. *There is no knee-jerk on either side, even with reinforcement.* This is especially noteworthy because of the spasticity in the lower limbs. The knee-jerk is not prevented by the spasticity, as the spasticity is comparatively slight when the limbs have not been irritated, and even without irritation of the limbs there is no knee-jerk. When the attempt is made to obtain the knee-jerk there is no contraction visible in the quadriceps muscle of either side. Ankle clonus is not obtained on either side. . . . Achilles jerk is absent on each side."

Marie[1] has said that the tendon reflexes are never absent in multiple sclerosis.

The difference in the condition of muscular tonus and of the tendon reflexes in my case is most extraordinary. Van Gehuchten[2] has paid much attention to the relation of the muscular tonus to the tendon

[1] Marie. Leçons sur les maladies de la moelle.

[2] Van Gehuchten. Journal de Neurologie, August 20, 1897, No. 16, p. 305.

reflex. He believes there is a certain parallelism between the two; but the parallelism does not always exist, and the tendon reflexes may be exaggerated when the muscular tonus is not exaggerated, or the tendon reflexes may be preserved when muscular atony is found, or they may be absent when muscular hypertonia or contracture exists. I shall not discuss the theories he advances to explain these conditions, as they do not seem to me to be sufficiently founded on fact.

Strümpell[1] also believes that exaggeration of the tendon reflexes is often, but not always, associated with hypertonia of the muscles.

On the other hand, Parhon and Goldstein[2] do not believe that the condition of the reflexes is independent of the condition of the muscular tonus, and they assert that hypertonicity never occurs when the reflexes are lost, unless the reflexes are lost because the rigidity is so great that no movement is possible. These views are held also by some American authors. I show by this case that the patellar reflex may be lost when hypertonicity of the lower limbs is present and when this abolition of the reflex is not the result of immobility of the limbs from excessive rigidity. I have not been able to obtain Parhon and Goldstein's original paper, and must depend upon an abstract.

It is possible that in my case the patellar and Achilles reflexes were lost because sclerotic areas existed in the regions in which these reflex arcs within the spinal cord were contained. In the upper lumbar region no sclerotic focus was found, but in the mid-lumbar region a sclerotic patch was found in each posterior column implicating the fibres of the posterior roots after they had entered the cord. These sclerotic patches disappeared in the lower lumbar region, but at this level a sclerotic patch was found on one side implicating the anterior horn and anterior roots within the cord. The sclerotic areas found in the sacral cord were probably the cause of the lost Achilles jerk, and, in addition, the degeneration of one of the popliteal nerves examined may indicate that some of the terminal portions of the peripheral nerves were diseased. This alteration of the nerve fibres of the peripheral nerve was probably secondary to the alteration of the cell-bodies of the anterior horns of the spinal cord. The loss of the tendon reflexes of the lower limbs seems easily explained.

The exaggeration of the muscular tonicity may have been caused by the implication of the pyramidal tracts in the sclerotic areas above the lumbar region. If the impulses from all parts of the lower limbs had been almost entirely cut off it seems hardly probable that the muscular tonicity would have been exaggerated. A slight interference with the sensory impulses concerned in the reflexes may, however, be sufficient

[1] Strümpell. Neurologisches Centralblatt, July 1, 1899, No. 13, p. 618.

[2] Parhon and Goldstein. Roumanie médicale, 1899. Abstract in Revue Neurologique, March 15, 1902, p. 223.

to cause a loss of these reflexes, even in association with hypertonicity. Doubtless sufficient sensory impulses passed to the cord to cause exaggeration of the tonicity when the pyramidal tracts were diseased and the inhibition from the brain was removed.

In combined systemic disease the posterior and lateral columns are degenerated, and in some cases the spasticity later yields to flaccidity, apparently because after a certain time sensory impulses from the limbs to the cord are almost cut off, and therefore the paralysis becomes flaccid, even though the lateral columns may continue to degenerate. In illustration I refer to a case reported by Rheinbaldt,[1] in which rigidity of the lower limbs was prominent in the commencement of the palsy of these limbs, but when the patient came under Rheinbaldt's observation the palsy had become flaccid. Systemic degeneration of the direct and crossed pyramidal tracts, of the direct cerebellar tracts, and of the posterior columns was found. Rheinbaldt refers to a still more satisfactory case reported by Rothmann,[2] in which rigidity of the lower limbs gave place within two months to flaccidity.

Raymond and Cestan[3] have reported a very interesting case of disseminated sclerosis with paralysis in the associated movements of the eyeballs. The eyeballs were in a median position, and there was no ptosis. The irides reacted well to light and in accommodation. In each lateral movement of the eyeballs toward the right or toward the left the cornea was arrested about 7 or 8 millimetres from the external angle. Convergence, however, was very slightly affected. A sclerotic plaque was found implicating the nuclei of the third and fourth nerves. They quote Parinaud as saying that these associated paralyses are common in multiple sclerosis, but are usually incomplete. The ocular paralysis in Raymond and Cestan's case was incomplete, as it was in mine, and the lesions in the ocular nuclei in the two cases were similar. In a note of June 24, 1901, by Dr. H. F. Hansell, regarding my case, the statement is made that there was paralysis of the third nerve of each side and almost complete ophthalmoplegia. Iritic response was good. The pupils were equal. There was partial atrophic cupping of both optic nerves, with reduction in size of the bloodvessels without signs of previous inflammation. Dr. Hansell, in answer to an inquiry made by me, says: "'Almost total ophthalmoplegia' means in this case that the sixth nerves were also involved. Had external rotation been preserved my expression would have been 'double third-nerve paralysis,' and the word 'ophthalmoplegia' would not have been mentioned. Again, the total third-nerve paralysis could not have been present, since the report states that the pupils were responsive to light."

[1] Rheinbaldt. Archiv für Psychiatrie, vol. xxxv., No. 1, p. 57.
[2] Rothmann. Deutsche Zeitschrift für Nervenheilkunde, vol. vii.
[3] Raymond and Cestan. Revue Neurologique, January 15, 1902, p. 52.

The implication of the sixth nerves in my case, as in Raymond and Cestan's, suggested a paralysis of associated movement resulting from the destruction of the connection by means of the posterior longitudinal bundle between the nuclei of the oculomotor nerves and those of the abducent nerves. This form of paralysis is known by the Germans as blicklähmung. In my case at least the sixth nuclei as well as the third and fourth were implicated in the sclerotic area.

EOSINOPHILIA IN PELVIC LESIONS AND IN THE VERMIFORM APPENDIX.

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In the routine microscopic examination of all tissues removed at operations in the gynecological service of the Lakeside Hospital, cells with eosinophilic granulations have frequently been observed in the tissues, especially in inflammatory conditions. In this laboratory their occurrence was first noted in the gynecological department in 1898, and subsequently so many instances were observed in all the departments of the laboratory that Howard and Perkins[1] were able to report a large number of cases. The present article deals with the material of the gynecological department alone.

Howard and Perkins in material from 825 consecutive operations in the different services of the hospital found eosinophiles in the tissues of 108 cases, or 13 per cent. Of these 80, or 74 per cent., were inflammatory; 24 cases were acute and 56 were chronic; 9 were tuberculous and 9 were syphilitic. In 120 consecutive autopsies eosinophiles in larger or smaller numbers were found in organs showing pathological changes in 27 instances. They occurred in the spleen, liver, stomach, intestines, kidney, heart, lung, thymus, lymph glands, and skeletal muscles.

These findings appear to warrant the conclusion that eosinophiles take an active part in many inflammatory processes, more especially appendicitis, pyosalpinx, and ovarian abscess, as well as in many cases of carcinoma showing inflammation; that they are often associated with polymorphonuclear neutrophiles and almost invariably with plasma cells; that their development from plasma cells and mononuclear leucocytes could be traced in many instances. These writers are of the opinion that the eosinophiles found in the tissues have usually

[1] Johns Hopkins Hospital Reports, vol. x.

emigrated from the vessels, but that in a certain proportion of cases they are formed in the lesion by transition from plasma cells and mononuclear leucocytes. Their article contains a careful review of the literature, of which two references are here applicable.

Przerwoski[1] noted them in 4 cases of carcinoma of the portio vaginalis, occurring in the connective tissue, in the carcinoma cell nests, and in the bloodvessels. He counted as many as five, ten, or fifteen in a single D D Zeiss field.

Feldbausch[2] found eosinophiles in uterine carcinoma and mammary cancer with acute mastitis, in metastases in lymph glands secondary to epithelioma of the vulva, in epithelioma of the bladder and of the lip, and in some sarcomata and lymphosarcomata. He gives many references, and quotes similar cases noted by Rimbach and Neusser.

As regards the technique employed, the majority of the tissues were fixed and hardened in Orth's fluid (Müller's fluid, 9 parts; 40 per cent. formaldehyde solution, 1 part), the best results being obtained after hardening in this for a week; they were then embedded in celloidin and stained with hæmatoxylin and eosin. The eosinophiles are also readily demonstrated after hardening with mercuric bichloride, formalin, Zenker's or Müller's fluids, and staining with hæmatoxylin and eosin, or with eosin followed by polychrome methylene blue or carbolic toluidin blue, or with the Biondi-Heidenhain triple stain. Tissues hardened in alcohol fail to show the eosinophiles satisfactorily. In specimens hardened in Orth's fluid and stained with methylene blue alone the granulations of the eosinophiles, although unstained, are plainly visible with the higher powers, while in alcohol hardened preparations, even after staining with eosin, they cannot be seen. Fine scrapings of the appendix mucosa, which almost invariably shows eosinophiles, were dropped into warm absolute alcohol with no better result. Parallel pieces of the same appendix were hardened in the usual reagents and stained as uniformly as possible. The eosinophiles were well shown after employing Orth's fluid, formalin, Zenker's and Müller's fluids, and mercuric bichloride, but they could not be found after using alcohol. The same results were obtained in a number of cases of thickened pyosalpinx when adjacent pieces of each were hardened in the different fluids.

Very satisfactory results were obtained with suitable tissues hardened in Orth's fluid and stained with eosin, followed by Unna's polychrome methylene blue or carbolic toluidin blue. The bacteria and nuclei are stained blue; the eosinophiles are very prominent, and are readily distinguished from the polymorphonuclear neutrophiles, whose protoplasm takes a slight pinkish tinge, and from the mast cells, whose large granu-

[1] Przerwoski. Centralbl. für Allgem. Patholog. und Path. Anatomie, 1896, vol. vii. s. 117.
[2] Feldbausch. Virchow's Archiv, 1900, clxi.

lations take the basic stain, being lilac-colored and darker than the bright-red eosinophilic granulations.

In inflammatory conditions the eosinophilic infiltration is usually most marked in suppurative cases or in the subacute stage. It occurs also in some recent acute and in chronic cases. These cells play a part in general cellular infiltrations in which polymorphonuclear neutrophiles, small round cells or lymphocytes, plasma cells, and mast cells also participate. The number of the eosinophiles varies within wide limits. Many of our cases showed them in the tissues, but in such small numbers that we have not included them in our list, while in others they were very numerous. Przerwoski[1] found as many as five, ten, or fifteen in a D D Zeiss field, but in several cases in selected areas we have counted as many as 250 in the smaller field of a 1/12 oil-immersion with an Oc. 4. They are usually polymorphonuclear, although mononuclear forms are also found. As a rule, they are spherical, but frequently are elongated and fusiform in shape, lying between the connective tissue or smooth muscle cells. Some of these fusiform cells may have but a few eosinophilic granulations and be mononuclear, the nucleus being vesicular and resembling those in the adjacent connective tissue cells. All intermediate forms between these and the polymorphonuclear spherical eosinophiles are seen, suggesting the possible formation of connective tissue cells from the eosinophiles, or *vice versa*. In such areas Howard and Perkins have traced the development of eosinophiles from smooth muscle fibres, and have shown that eosinophiles may be derived from plasma cells and large mononuclear leucocytes, and describe a progressive series of cells intermediate between these. We have observed these forms, but we have also frequently seen a similar series of cells intermediate in type between the plasma cell and the mast cell of the tissues, especially in the appendix mucosa, stained with Unna's polychrome methylene blue, carbolic toluidin blue, or either of these after eosin. The first stage is the formation of fine granulations in the plasma cell, which gradually become larger and stain more deeply until the typical mast cell of the type found in the tissues is reached. Whether or not this be an indication of the development of mast cells from plasma cells, or *vice versa*, the demonstration of an intermediate series of cells is at least of interest.

The pathological material upon which these observations are based was all obtained from the first 500 consecutive operative cases in which tissues were removed in the gynecological service of the Lakeside Hospital. In 145 of these cases infiltration with eosinophiles was found. The tissues from 261 of the 500 cases were hardened in alcohol, and

[1] Przerwoski. Loc. cit.

therefore would not have shown eosinophiles even had they been present; 248 of these 261 cases supplied endometrium alone or with portions of the cervix. There are left, then, only 104 cases in which appropriate fixing agents were employed and in which eosinophiles were absent or found only in small numbers. The majority of these were chronic inflammatory cases.

The 145 cases with eosinophilic infiltration showed the following pathological conditions, which are arranged in the order of their frequency, the numbers indicating the number of cases in which each condition was found. The total would greatly exceed the number of cases, from the fact that several different pathological conditions showing eosinophilic infiltration often occurred in the same patient.

Appendix, normal and diseased	56	Omentitis	4
Pyosalpinx	54	Tubal pregnancy	3
Salpingitis	33	Normal corpus luteum	3
Ovarian abscess	25	Sarcoma uteri	3
Perioöphoritis	17	Interstitial cervicitis	3
Corpus luteum cyst	12	Fibro-adenoma of the breast	2
Congestion of the Fallopian tube	11	Proctitis	2
Endometritis interstitialis	10	Malignant adenoma uteri	1
Carcinoma of the cervix	11	Suppurative metritis	1
Hydrosalpinx	6	Fibromyoma uteri	1
Oöphoritis	4	Syphilitic elephantiasis of the vulva	1

These conditions will now be considered more in detail.

Pyosalpinx was the most frequent inflammatory condition showing eosinophilic infiltration. In the 500 cases pyosalpinx was found 62 times, being usually bilateral; 54 of these cases showed eosinophiles in the tissues in large numbers; in 4 cases only a few of these cells were found, in 2 of which the tissues were imperfectly hardened, while a third showed marked eosinophilic infiltration in the other tissues removed; in 4 cases they were absent, the tissues in 3 of these having been hardened in alcohol.

The infectious agent in the majority of these cases, and in fact in most pelvic inflammatory conditions, was undoubtedly the gonococcus. In a number of instances typical gonococci were found on cover-slip examination of the pus and also in stained sections of the tissue; in many others, although the history was extremely suggestive, cover-slip examination and cultures of the pus proved negative, thus confirming the statement that in many cases the pus is either sterile or of slight virulence. Streptococcus pyogenes, bacillus mucosus capsulatus, staphylococcus pyogenes albus, and bacillus tuberculosus were the causal agents in some of the above cases.

In pyosalpinx the eosinophiles are most numerous in the muscularis, especially where this is considerably thickened. Here they are often seen assuming a spindle form and crowded into rows between the muscle and connective tissue cells. They are seen more sparsely in the stroma

of the folds, in the purulent exudate, and in the vessels; they are never so numerous in the folds as in the muscularis. In the vessels the leucocytes are often increased in number, but the percentage of eosinophiles is usually about normal, although on account of their more prominent appearance the proportion seems increased. Since the histological findings in most of these cases are very similar, a short description of one will suffice.

Gynecological Pathological, No. 465. Right perioöphoritis and pyosalpinx; left ovarian abscess and pyosalpinx. The left tube, 8 cm. in length, is much thickened, convoluted, and occluded. The lumen is distended with pus showing typical gonococci; the outer surface of the tube is covered with dense adhesions.

Microscopically the lumen contains a quantity of pus, gonococci being seen in some of the cells. The folds of the mucosa are numerous, showing a complex arrangement, but only a few adhesions. As a rule, they are greatly thickened and swollen, exhibiting dense cellular infiltration, with polymorphonuclear neutrophiles, lymphocytes, plasma cells, eosinophiles, and mast cells. The epithelium is almost everywhere intact, but is pale, swollen, and cuboidal, being scarcely distinguishable from the connective tissue cells of the folds. The cilia are usually missing, and numbers of leucocytes are found between the epithelial cells. On the more normal folds the epithelium is intact, almost normal, and shows cilia.

The muscularis is greatly thickened. The muscle cells are pale and swollen. There is a considerable increase of connective tissue and a diffuse cellular infiltration, especially with the eosinophiles, which frequently exceed 10 per cent. of all the cells in the field. Large numbers of polymorphonuclear neutrophiles, lymphocytes, and plasma cells, with fewer mast cells, are also found. The peritoneum is found beneath thick adhesions, where it forms atypical groups of pale, swollen cells.

Salpingitis, without pus formation, showed eosinophilic infiltration in 33 cases; 6 of these, although diagnosed as acute salpingitis, contained microscopically a small amount of purulent fluid in their lumina, and might come under the head of pyosalpinx; in all 6 the eosinophiles were found only in the mucosa and in small numbers, their favorite site, the muscularis, being almost normal in appearance. In salpingitis the eosinophiles are usually less numerous than in pyosalpinx, and occupy the wall of the tube in subacute cases. In many cases of chronic or "healed" salpingitis all acute cellular infiltration had disappeared, and hence eosinophiles were absent. The following case is instructive:

Gynecological Pathological, No. 305. Supravaginal hystero-salpingo-oöphorectomy for multiple fibromyomata uteri. Both ovaries and tubes macroscopically normal. Microscopically, in the right tube the lumen is empty; the mucosa is normal except for slight eosinophilic infiltration in some of the folds, which are numerous and show a normal arrangement. The surface epithelium is intact, the cells being columnar and ciliated. The muscularis shows very marked cellular infiltration,

almost entirely with polymorphonuclear eosinophiles, which are usually accumulated in masses in the connective tissue between the muscle bundles. In some fields of a 1/12 oil-immersion lens with Oc. 4, over 90 per cent. of all the cells seen are eosinophiles, as many as 250 being counted in one such field without change of focus, although an adjoining field often shows a total absence of them. This infiltration is entirely missing in about one-third of the muscularis encircling the mucosa, and in the other two-thirds no other pathological change is found. If it were not for the actual presence in the tissues of the leucocytes a diagnosis of congestion would have been made instead of acute salpingitis.

Congestion due to traumatism at operation was found in tubes presenting a normal appearance, but which were removed with uterine fibromyomata, ovarian cysts, or some condition not involving the tube itself. Microscopically the only change found in these cases is a congestion of the vessels, with an increased number of leucocytes within their lumina. The eosinophiles, while actually more numerous than normal, preserve the usual ratio to the other leucocytes, although, owing to their more prominent staining, the former appear increased. In all cases showing such congestion the eosinophiles were sufficiently increased to attract attention.

Hydrosalpinx was present in 23 of the 500 cases. In the majority of these the changes were slight in degree and chronic, all acute cellular infiltration having disappeared. This would readily account for the fact that in only 6 cases were eosinophiles demonstrated.

Tubal pregnancy was found 5 times. In 3 there was moderate eosinophilic infiltration; in another but few were found, the condition being very chronic; a pyosalpinx, however, upon the other side showed abundant eosinophilic infiltration. The tissues from the fifth case were hardened in alcohol, and showed no eosinophiles.

Ovarian abscess was present in 27 cases, in some of which the condition was bilateral. Eosinophiles were seen in large numbers in the abscess wall in all but 2 cases; in these the tissues had been hardened in alcohol. Although in many of these cases there was a definite gonorrhœal history, the specific organisms could rarely be demonstrated. The streptococcus pyogenes was found in 2 cases. One case only will be quoted, the others presenting very similar findings.

Gynecological Pathological, No. 394. Left perioöphoritis and salpingitis; right ovarian abscess and pyosalpinx. The right ovary—5 x 3.5 x 2 cm.—is of soft consistence, and shows a number of surface adhesions. On section, an abscess sac is found in its interior. The right tube is occluded, filled with pus, and densely adherent to the ovary; together they weigh 31 grammes. Microscopically, the medulla of the ovary is for the most part replaced by an abscess which appears to have formed in a corpus luteum. The abscess wall is abundantly supplied with small vessels, and shows dense cellular infiltration, especially with eosinophiles, but also with polymorphonuclear neutro-

philes, lymphocytes, plasma cells, and fewer mast cells. The eosinophiles are most numerous in the abscess wall about midway between the inner necrotic border and the sound tissue outside. They give a reddish tinge to the tissue when seen with the lower powers, and in selected areas with a 1/12 oil-immersion lens and a No. 4 ocular they sometimes represent 60 to 75 per cent. of all the cells, as many as 150 having been counted in one such field. These cells are also found in less numbers in the pus within the abscess cavity, in the cortex and tunica albuginea, and within the vessels.

Perioöphoritis representing either an acute exudation or chronic adhesions was found in 121 cases. The majority of these were chronic, and showed no acute cellular infiltration. Eosinophiles were found in only 17 of the acute or subacute cases, often associated with pyosalpinx.

Oöphoritis showing eosinophilic infiltration was found in only 4 cases.

Excluding ovarian abscess and perioöphoritis, cellular infiltration of the ovary itself is uncommon, the inflammatory process being held in check apparently by the dense tunica albuginea, as is shown in many cases of acute perioöphoritis, where the cellular infiltration is found only in the exudate upon the surface.

Corpora lutea of normal appearance in three cases showed a number of eosinophiles associated with the usual increase of the connective-tissue elements in the later stages of the corpus luteum.

Corpus luteum cysts frequently show a slight cellular infiltration in their walls which can scarcely be termed an oöphoritis. In 12 such cases eosinophiles formed a considerable proportion of the infiltrating cells. Some of these cases probably represented enlargements of the Graafian follicles, with loss of the membrana granulosa, as it is frequently impossible to differentiate the two conditions.

The endometrium showed eosinophiles in small numbers in 10 cases of interstitial endometritis; in interstitial inflammation of the cervix they were found 3 times. These numbers seem small, but the majority of these tissues was hardened in alcohol, since it is difficult to separate the clot from the tissue if Orth's fluid be used. At present, however, we employ formalin. Of the 500 cases, in 248 the tissues represented endometrium alone or with portions of the cervix hardened in alcohol.

Metritis. Six cases of very slight metritis did not show eosinophiles, but in 1 of suppurative metritis they were numerous. The following is an illustrative case:

Gynecological Pathological, No. 295. Uterus septus partialis; acute interstitial endometritis; suppurative metritis; left tubo-ovarian abscess; right salpingitis and oöphoritis; adherent appendix. The uterine wall upon the left side was riddled with small abscesses, the pus from which showed streptococci on cover-slips and cultures. Eosinophiles were very numerous in the abscess wall.

Carcinoma of the cervix occurred in 16 of the 500 cases. In only 1 of these was a hysterectomy performed, the remaining cases being so far advanced as to warrant merely a palliative curetting, which in some cases was repeated at a subsequent date. Eosinophiles were found in large numbers in 11 of the 16 cases; they were absent in 5, in 2 of which the tissues were hardened in alcohol. The favorite seat of the eosinophiles is along the advancing margin of the growth. One instance will be cited.

Gynecological Pathological, No. 319. Vaginal hysterectomy for carcinoma of the cervix occurring in a nullipara. Microscopically in this specimen the cell nests as well as the interstitial connective tissue show dense eosinophilic infiltration, most intense along the advancing margin, where they give the tissue a reddish color when seen with the lower powers. In some fields of a 1/12 oil-immersion lens more than 90 per cent. of the cells seen are eosinophiles.

Malignant adenoma of the body of the uterus was found in the material from two operations upon the same patient. Curetting was first done for diagnosis, and subsequently hysterectomy was performed. The disease was in a very early stage, and did not involve the muscularis; the eosinophilic infiltration was slight. The condition corresponded with the malignant adenoma described by Gebhard[1] as distinguished from adenocarcinoma.

Sarcoma Uteri. Three cases occurred, and have been reported in a recent article.[2] In all, eosinophiles were found among the sarcoma cells and in the muscularis of the uterine wall near the advancing neoplasm. They were not so numerous as in carcinoma of the cervix.

Fibromyomata uteri were represented in 25 of the 500 cases; in 1 eosinophiles were found associated with areas of hyaline degeneration of the tumor.

Chronic syphilitic inflammation of the labium minus—the so-called elephantiasis syphilitica—occurred once in our series. There was a great increase of fibrous connective tissue, marked endarteritis, and considerable cellular infiltration, in which eosinophiles occurred in moderate numbers.

Fibro-adenomata of the breast were removed in 2 cases as supplementary procedures to other operations. They were both small, and showed areas of myxomatous degeneration. No inflammatory process was found microscopically, but in Gynecological Pathological, No. 475, a typical intracanalicular fibro-adenoma; these cells were fairly numerous, usually mononuclear, and scattered throughout the stroma. The other case showed but few.

Vermiform Appendix. This was removed frequently as a secondary procedure to some other abdominal operation. In many of these cases

[1] Gebhard. Patholog. Anat. der Weibliche Sexualorgane, 1898.

[2] Weir. American Journal of Obstetrics and Diseases of Women and Children, 1901.

it showed but slight pathological change, such as light surface adhesions, concretions in the lumen, or sharp twists from shortening of the mesoappendix. Upon microscopic examination the greater number of these appeared perfectly normal. The occurrence of eosinophiles in the mucosa of the normal or diseased appendix is almost invariable, and as a number were examined the findings are included in this paper.

In the 500 cases the appendix was removed 69 times, and eosinophiles were found in considerable numbers in 56. Their absence in the remaining 13 is explained by the fact that in 11 the lumina were occluded, and the mucosa, in which the eosinophiles are found, was entirely replaced by connective tissue; the remaining 2 specimens were hardened in alcohol. Of the 56 showing eosinophiles 47 were microscopically normal, although 4 of these contained firm concretions in the lumen and another contained two grape-seeds; 5 showed inflammation in varying degree, 1 contained pus, the remainder showing periappendicitis. In 2 myxomatous degeneration of the mucosa was found, 1 of these being quite cystic. Another case showed cystic dilatation above a narrow constriction, and in the remaining case the appendix was occluded, the epithelial elements were entirely lacking, but some of the lymphoid tissue still remained and showed eosinophiles. One case will be mentioned.

Gynecological Pathological, No. 393. Left salpingo-oöphorectomy and appendectomy. The appendix, 8 cm. in length, was perfectly normal except for a sharp flexure due to a shortening of the mesoappendix. Microscopically a considerable proportion of the cells composing the stroma of the mucosa are polymorphonuclear eosinophiles. They represent fully 10 per cent. of all the cells, and in some fields with a 1/12 oil-immersion lens they reach 30 to 50 per cent. They are most numerous in the deeper layers around the bases of the tubular glands, but are absent in the lymphoid nodules. They are usually polymorphonuclear, but a few are mononuclear. They are, as a rule, spherical or oval in shape, but also flattened or irregular in outline. Owing to the whole cell being stained, their number seems even larger than it really is. Polymorphonuclear neutrophiles are very scanty in the mucosa, but many plasma cells and some mast cells are found.

Rectum. In 2 cases with dense adhesions portions of the rectal wall were torn away at operation. Microscopically these showed large numbers of eosinophiles in the mucosa, and also forming part of a diffuse cellular infiltration throughout the whole bowel wall. Mast cells are found in much smaller numbers.

Omentum. Frequently at operation small portions of the torn or adherent omentum required resection. In 7 cases it showed an inflammatory condition. Eosinophiles were found in considerable numbers in 4, in small numbers in 1. In the remaining 2, where the inflammatory condition was very slight, they were missing.

Circulatory Eosinophilia. An increased number of eosinophiles in the circulating blood is said to occur in certain pelvic lesions, 4 per cent. of all the leucocytes being considered the maximum normal number of the eosinophiles.

Cabot[1] says that in carcinoma of the uterus with a leucocytosis the eosinophiles in the blood are not always decreased (as they are in many other leucocytoses), nor are they increased except when bone metastases occur. He also states that in gonorrhœal infection and in many ovarian tumors there is frequently an eosinophilia, while in most leucocytoses there is a decrease of eosinophiles.

Ewing[2] also states that there may be an eosinophilia in gonorrhœal infection.

Ehrlich and Lazarus[3] admit a moderate eosinophilia in some malignant tumors.

Vosswinckel,[4] who made differential counts in a large number of cases of disease of the female genitalia, concluded that:

1. A circulatory eosinophilia is absent in diseases of the tube alone. In pus cases there may be an increase in the polymorphonuclear neutrophiles, but no myelocytes are found. In 30 cases of fibromyomata a circulatory eosinophilia did not occur, nor was it noted in 23 cases of endometritis. In both of these latter conditions, however, a leucocytosis may occur.

2. In all severe diseases of the ovary, with fever, except carcinoma of the ovary, there is a circulatory eosinophilia.

3. In the majority (10 out of 18) of cases of large ovarian cysts and suppuration of the ovary causing extensive degeneration there is a circulatory eosinophilia, and myelocytes are also found.

4. In carcinoma of the uterus the eosinophiles in the blood may be increased, normal, or decreased, there being no difference between mild and severe cases.

Vosswinckel also quotes the following:

Neusser found in ovarian disease that the eosinophiles were increased, and that the myelocytes, which are not found in normal blood, are also found.

Kopp in 5 out of 16 cases of pelvic disease found an undoubted circulatory eosinophilia.

Zappert found the eosinophiles in the blood increased in 2 cases of carcinoma of the uterus and in 1 case of sarcoma of the ovary; decreased in 1 carcinoma of the ovary.

[1] Cabot. Clinical Examination of the Blood.
[2] Ewing. Clinical Pathology of the Blood, 1901.
[3] Ehrlich and Lazarus' Die Anämie. Nothnagel's specielle Path. und Therapie, 1901.
[4] Ueber das Vorkommen von eosinophilian Zellen und Myelocyten in menschlichen Blute, Monats. für Geburtshülfe und Gyn., 1899.

Reinbach in 40 cases of malignant tumors found the eosinophiles in the blood lessened in only 1 case of carcinoma of the ovary and stomach.

Our own observations on this point are limited, but as far as they go we have found that more than 4 per cent. of eosinophiles in the blood in pelvic diseases is quite uncommon. In most instances the counts were made in the inflammatory conditions associated with leucocytosis, and in most of them the eosinophiles were decreased in number, confirming Cabot's statement. In 29 of the cases showing eosinophilic infiltration of the tissues 48 differential counts were made, and in only 3 cases was a circulatory eosinophilia found.

Gynecological Pathological, No. 349. Bilateral chronic hydrosalpinx and perioöphoritis. Leucocytes, 4800; eosinophiles, 5.12 per cent.

Gynecological Pathological, No. 124. Right perioöphoritis and hydrosalpinx; left perioöphoritis and pyosalpinx. The day before the operation the leucocytes were 20,000, with 4 per cent. of eosinophiles. Two days after operation the leucocytes had fallen to 12,000, with 5 per cent. of eosinophiles.

Gynecological Pathological, No. 63. Left ovarian abscess and pyosalpinx (streptococcus); right perioöphoritis and salpingitis. Leucocytes, 8666; eosinophiles, 5 per cent.

Four per cent. of eosinophiles occurred but once, in a case of bilateral gonorrhœal ovarian abscess and pyosalpinx, with a leucocytosis of 16,900; 3 per cent. of eosinophiles was found twice, in one case of bilateral gonorrhœal ovarian abscess and pyosalpinx, with a leucocytosis of 9740, and in a case of bilateral gonorrhœal pyosalpinx, with a leucocytosis of 9260.

In the remaining 23 cases 41 counts were made. In 20 counts made in 12 cases the eosinophiles were 2 per cent. or a fraction over; in 11 counts made in 11 cases the eosinophiles were 1 per cent. or a little over; in 10 counts made in 10 cases the eosinophiles were below 1 per cent. In all examinations at least 400 leucocytes were counted, and in none were myelocytes found. These counts were nearly all made immediately before operation. In some cases subsequent examinations were made on the first and second days after operation. A considerable number of differential counts were made in cases in which no eosinophilic infiltration of the tissues was found or in which operation was refused. The only one of these showing an increase of eosinophiles in the blood was an advanced carcinoma of the cervix. In this case 7.5 per cent. of eosinophiles were found.

Conclusions. 1. Eosinophiles take a prominent part in the cellular infiltration associated with inflammatory and suppurative processes of the pelvic organs.

2. In such conditions they usually occur in the largest numbers in the subacute stage and associated with connective tissue hyperplasia.

3. Eosinophilic infiltration is found in most cases of carcinoma of the cervix and in almost all cases of pyosalpinx and ovarian abscess.

4. In inflammatory conditions of the endometrium eosinophiles occur in small numbers and in but few cases.

5. Eosinophiles represent a large proportion of the cells forming the stroma of the mucosa in the normal and the diseased appendix.

6. In inflammatory conditions of the pelvic organs associated with an eosinophilic infiltration of the tissues the percentage of eosinophiles in the circulating blood is rarely increased, and usually decreased.

I am much indebted to Dr. William T. Howard, Jr., Professor of Pathology, and Dr. Hunter Robb, Professor of Gynecology, for kindly advice and permission to make use of the pathological material.

THE PATHOLOGY OF THE TISSUE CHANGES INDUCED BY THE X-RAY: PRELIMINARY REPORT.

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The therapeutic efficacy of the X-ray is apparently demonstrated by the results in hundreds of cases of epithelioma, lupus, sycosis, acne, and other lesions thus treated, though time is yet needed to establish the permanency of the cures reported. The clinical effects are much the same in all successful cases—lessening or cessation of pain, drying of discharge if present, smoothing of roughened surfaces, formation of scar tissue. In the case of tumors covered by the skin there is a gradual diminution in size, accompanied or not by softening. The result of overexposure or idiosyncrasy—the so-called X-ray burn—is a well-known, but now, fortunately, very rare complication. Some writers[1, 2] claim that a reaction, evidenced by a slight dermatitis or its equivalent, is necessary or desirable to obtain therapeutic effects from the X-ray, while others[3, 4, 5, 6] agree in the belief that this is not essential.

The nature of the tissue changes induced by the X-ray in producing its effects is not clearly understood. Many explanations are offered. Some of these are based on microscopic studies of tissue; others have a clinical foundation, while the only apparent basis of a certain number is the idle speculation of a fertile imagination. With the desire of adding to the knowledge of this question the writer has studied microscopically several tumors, both before and after a series

of exposures to the X-ray. This article embodies the results of these studies as well as a brief résumé of the theories and findings of other workers gained during a somewhat extensive, though not complete, examination of the more recent literature on the subject.

Oudin, Barthelemy, and Darier,[7] in a study of X-ray alopecia in guinea-pigs, found the prickle-cell layer and the stratum granulosum ten to fifteen times thicker than the normal, the individual cells being little altered. Not a single hair was visible, and there were only traces of follicles. Hair papillæ, regeneration buds, hair muscles, and sebaceous glands were lacking. The changes in the dermis were trivial compared to those of the epidermis, the connective tissue and elastic tissue networks being normal. The small as well as the large blood-vessels of both cutis and subcutis were normal, and no changes in the nerve fibres were observed. These writers conclude that the X-ray is an irritant of unusual strength, and seems to increase the vitality of the least differentiated skin elements. On the contrary, the differentiated elements—hair, nails, and glands—undergo retrogressive changes and atrophy. They do not know whether these changes are due to nervous influence or to obliteration of vessels or other circulatory disturbances.

Huntington[8] quotes Rudis-Jicinsky as stating that in the X-ray burn the lesion consists of an acute, subacute, or chronic necrobiosis. In a later article Rudis-Jicinsky[9] says: "The irritation of the peripheral extremities of the sensory nerves causes a paralysis of the vasomotors of the vascular area affected, spasmodic contraction of the arterioles and capillaries follows, and the proper nutrition of the cells is impaired. . . . With these changes, which are directly dependent upon disturbance of the circulation, there are changes in the parenchyma cells of the affected region. The death of tissue follows, being caused by permanent stasis in the bloodvessels." Huntington also quotes Gassman and Schenkel as finding the intima of arterioles and veins, especially the latter, appreciably thickened and the lumen correspondingly narrowed. This, it is claimed, is due to a deposit of reticular masses of delicate fibrous tissue. Similar processes were noted in the elastica and muscularis.

Lowe[10] mentions Lord Kelvin's demonstration of the fact that an iron bar, electrified and insulated, can be discharged or de-electrified by the X-ray. He is of the opinion that the dermatitis as well as the therapeutic results may depend upon some similar action on the trophic nerves of the parts exposed.

Veliaminoff[11] states that Glebovski noted an increase in fibrous tissue, with conspicuous elastica, in cases of lupus and rodent ulcer treated with the X-ray, and also that lymphoid and giant cells underwent fatty degeneration.

Codman[12] coincides with the opinion that attributes these lesions to a primary action on the trophic nerves of the bloodvessels and skin. "The delay in the appearance of the lesions after the exposure, their progressive character, and their failure to react to stimulating treatment are the strongest reasons for this view. The reports of microscopic examination of the excised tissue agree in stating that the smaller arterial branches are occluded, and the appearances are not unlike those of necrosis and inflammation due to other causes."

Pusey[13] says that carcinomatous masses are replaced by a degenerated, wavy substance without structure and staining a faint blue with hæmatoxylin. The contour of the epithelial cells is lost, and cell nuclei disappear. It is a "degenerative process of some sort, what, cannot be said."

Scholtz[14] says that the X-ray affects, first or entirely, the cell elements which undergo a slow degeneration. This is shown chiefly in the epithelial cells. The phenomena of this degeneration are manifold, the nucleus as well as the protoplasm of the cell being affected. Inflammatory phenomena appear when this degeneration reaches a certain stage. Vessel changes have probably much to do with the further progress and slow healing of ulceration.

Walker[15] has studied sections of a rodent ulcer healing under treatment by the X-ray, and describes the new growth as undergoing fibromyxomatous degeneration.

Blackmar[16] concludes that the X-ray causes a breaking down of malignant and non-malignant growths, the disintegrated material being absorbed. He considers the waste products from a rapidly disintegrating cancer exceedingly dangerous when thrown into the general system unless the patient is in vigorous health.

Morton[17] believes that the effect of the X-ray in the cure of disease is due to a primary chemical reaction affecting in turn the metabolic processes. He claims that under proper conditions of administration the X-ray builds up tissue, in proof of which he cites the case of a young woman treated for enlarged axillary glands. In six weeks the neck, shoulders, chest, and breast of that side had developed so markedly that the patient afterward desired the opposite side treated to restore symmetry.

Beck[18] states that an adenocarcinoma subjected to X-ray treatment showed beginning colloid degeneration, changes of the same nature being observed in the epithelium of the skin covering the tumor. Integumental specimens show thickening of the tunica intima of the small bloodvessels, fibrous tissue in reticular arrangement being deposited. The same observer[19] elsewhere states that he places before all the nutritive changes in the walls of bloodvessels and the results incident to such changes.

Bean[20] does not think the change is a destructive one. He believes that the cells are restored to their normal condition; and while there may be and often is atrophy connected with the process, there is no necrosis. This statement he contradicts later by saying that in the light of the theory he advances, X-ray burn (really a dermatitis) is what should be expected as the result of too prolonged stimulation, and the necrosis which sometimes follows the dermatitis is the logical outcome of intense inflammation. The theory referred to is based upon the principle of molecular or atomic vibration and its response to heat and light. Bean reasons that the atomic movements of cancer cells and epithelial cells, or of sarcoma cells and connective tissue cells, are not greatly different. If a cell has not wholly departed from its proper atomic motion, we might expect the restoration of that motion or a return to the normal. As the X-rays are probably ethereal vibrations of high frequency, they act by restoring this lost motion to the cell.

Lancashire[21] says the therapeutic effect is due to mechanical stimulation. The process partakes of the nature of an inflammation.

Loeb[22] after seven exposures of ten minutes each during eleven days (transplanted sarcoma in a rat) found mitoses in the cells. The tumor continued to grow, and pieces from it were successfully transplanted into other rats. Degenerative changes were present in the centre of the tumor, but Loeb states that these changes take place in many tumors without exposure to the X-ray. They were perhaps increased by such exposure.

Herzog[22] treated transplanted sarcomas in two rats. The skin over the tumor became necrotic in each case. In one the tumor changed to a cyst filled with a perfectly clear fluid material, and after the fifth exposure the whole tumor came away, leaving a clean surface.

Wiesner[23] claims that the X-ray can act as an irritant to the nervous system, as shown by two cases in which after long exposure of the head to the rays there followed headache, dizziness, vomiting, and diarrhœa. Vomiting and diarrhœa have also followed exposures in the region of the stomach. He concludes that negative ions coming out of the tube penetrate the skin and undergo a chemical change in the molecules or in the nerve endings; this indirectly causes a trophic disturbance. The skin changes are to be looked upon as secondary. This explains the long incubation period of X-ray "burn" and the inaction upon it of therapeutic agents.

Dr. W. M. Sweet, in a personal communication to the writer, assigns to the X-ray a marked effect upon the nerves of exposed areas. In support of this view he mentions the rapid disappearance or lessening of pain in nearly every case treated. In Case II. of this series he removed with a scalpel the projecting portion of the tumor—a mass 2.5 x 3.5 cm. in dimensions—without the aid of anæsthesia and with

absolutely no pain to the patient. He also mentions the case of a prominent neurologist who received four four-minute exposures in the effort to locate a supposed foreign body in the eye. Following these the left side of the face became thoroughly anæsthetic to pain and to touch, sensation of heat and cold not being disturbed. The hair also fell out, but later returned. The anæsthesia rapidly diminished.

Hallopeau and Gadaud[24] call attention to the sclerogenic action of the X-ray, to which property they attribute the ungual dystrophies and vascular dilatations produced thereby.

Rinehart,[25] after stating that he gets no results from X-ray treatment unless inflammatory action is induced, continues: "It then remains to be decided whether the inflammation causes the death of the cancer cells and tuberculous deposits or whether the effect is produced by the light itself. My own opinion is that it is the light. Simple inflammation has often been caused by caustics in and around these sores of lupus and epithelioma without producing the death of the process. A light sufficiently strong to produce an inflammation of the healthy cells of the part treated is of sufficient strength to destroy cells of lower vitality, as cancer cells are known to be. Whether the effect upon the skin is produced by the ultra-violet rays remains to be proven. That the low vacuum tube produces more effect upon the skin than the high vacuum tube might help to substantiate the statement that the effect is from the ultra-violet rays, as they are given off more freely from a low vacuum tube."

Freund[26] in an article read at the British Medical Association states that in lupus and epithelioma the improvement is due to cell infiltration and proliferation and to the influence of the X-ray in promoting the formation of connective tissue and cicatrices. In his opinion the X-ray possesses no bactericidal qualities.

Bondurant[27] states his belief that the effect of the X-ray on cellular metabolism is the essential element in determining its value in the cure of disease, and not its destructive action (of which X-ray burn is an example), nor any supposed germicidal power.

McCaw[28] reports the apparent cure of a primary epithelioma of the uvula and soft palate by the use of the X-ray after excision and curettement. After twenty exposures a portion of the remaining growth showed degeneration of the epithelial cells, the protoplasm of which was almost entirely replaced by colloid material. This was not shown in the specimen examined before treatment.

Hett[29] believes that destruction of neoplasms does not really occur, because necrosis, if the X-ray is properly applied, does not take place in the cell. On the contrary, the cells seem to have an increased instead of a diminished vitality, this restoring the tissues to their normal condition. This statement seems difficult to reconcile with the

following, made a few paragraphs later: "It is a well-known fact that oxygen is set free by the X-ray, and it is probably this factor that produces a change in the neoplasm and embryonic cells by producing disintegration."

Pernet[30] examined irradiated lupus vulgaris tissue from beyond the obviously diseased periphery. The area had been subjected six months previously to fourteen consecutive daily exposures of ten to fifteen minutes each. In some parts the collagen was disjuncted and to some extent disintegrated. The greater part of the elastin had been destroyed. Sweat glands showed surrounding infiltration and signs of disintegration. The hair follicles and sebaceous glands had also apparently disappeared. A large vessel in the subcutaneous stratum showed thickening of its walls. In places there was a fibrous change in the upper layers of the corium.

Leonard[31] says that the X-ray has both a stimulating and an alterative effect on normal tissues. On tissues of low vitality it has an alterative effect. There may be caused a retrograde metamorphosis, ending in fatty degeneration.

Rieder[32] has demonstrated an inhibitory and distinctly bactericidal action of the X-ray on artificial cultures, and the case reported by Shand[33] might suggest this effect on bacteria in tissue. The lesions in Shand's case were recurring superficial abscesses of eighteen months' duration, the pus containing the staphylococcus pyogenes aureus. Improvement began under X-ray treatment, a relapse occurring when treatment was discontinued. Irradiation was again begun and continued until permanent cure resulted.

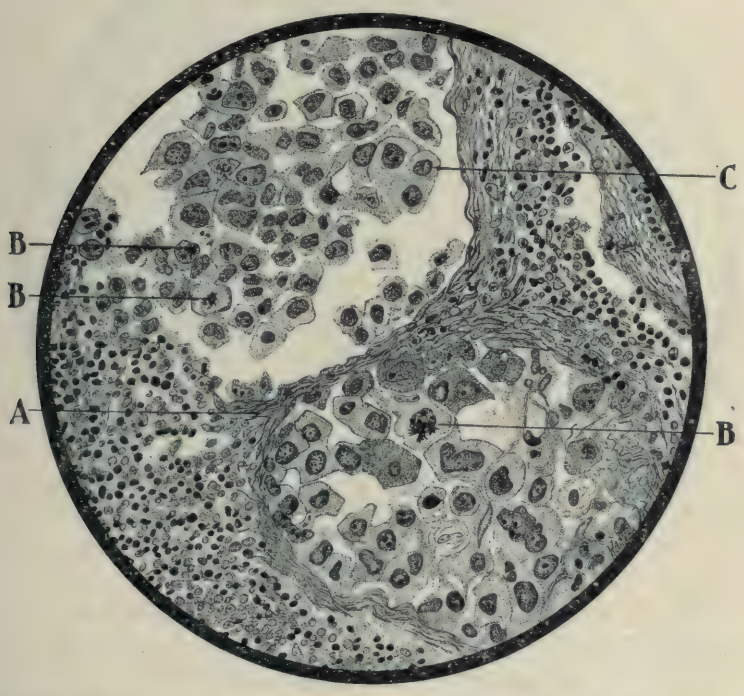
To this brief summary the writer wishes to add the following observations. For the material upon which the studies were made he is indebted to Dr. J. Chalmers Da Costa and Dr. W. M. Sweet. He also wishes to acknowledge the assistance in the study of tissue and preparation of this report rendered him by Dr. W. M. L. Coplin, who also suggested the idea and method of securing exposures of only a part of the tumor in Case I. This was accomplished by the use of a lead shield in which was made an opening corresponding in size and shape to the part to be exposed. By orienting this opening with the nipple at each application comparatively accurate placing was obtained, the exposed area being outlined with caustic at the time of the last exposure. Before the breast was removed two deep silkworm-gut sutures were passed to anchor the skin firmly to the underlying tissues, and before the removed specimen was incised the skin was further immobilized by inserting a row of sutures in the boundary of the outlined area.

In the examination of the tissues upon which this report is based the following technique was employed: Tissue, except that for study of the

nerves, was fixed in corrosive sublimate solution, hardened, and dehydrated in alcohol, and infiltrated with paraffin. Sections were stained with hæmatoxylin and eosin, hæmatoxylin and picric acid, and hæmatoxylin and Van Gieson; also with toluidin blue, Weigert's elastic tissue stain, Ehrlich's triacid mixture, and by Pianese's stain for differentiating hyalin, mucin, and colloid. Tissue for nerve study was fixed in Müller's fluid, dehydrated in alcohol, and infiltrated with celloidin, sections being stained by Weigert's method for myelin. Other pieces of the nerves were prepared by the method of Marchi.

CASE I.—M. W., aged forty-five years, patient of Dr. Da Costa. A tumor in the left breast was first noticed in July, 1901. This increased in size until February, 1902, when it was the size of a hen's

FIG. 1.



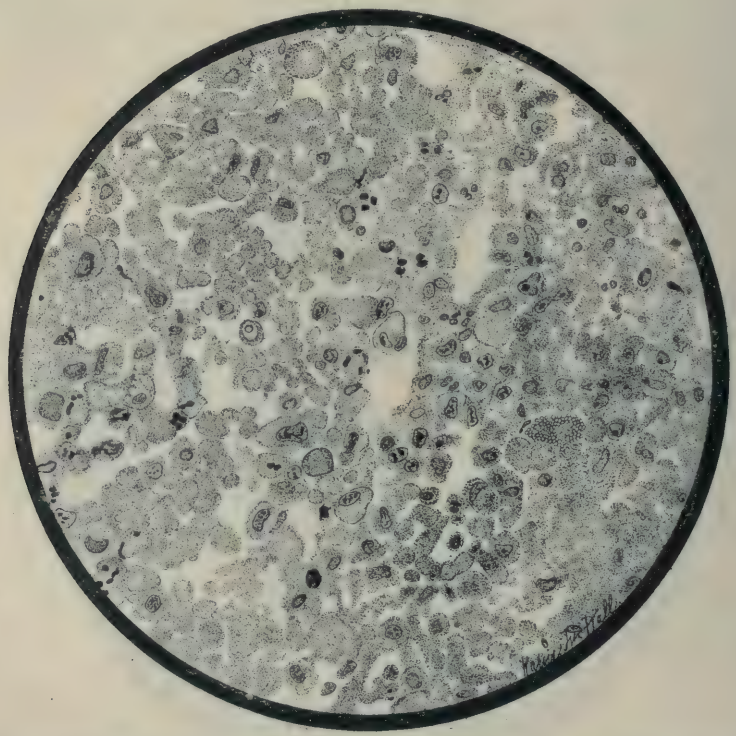
CASE I.—Scirrhous carcinoma of mamma. Section from unexposed area. A. Scanty stroma separating two alveoli. In the upper right and lower left parts of the field the extensive lymphoid and plasma-cell infiltration of the stroma is well shown. B, B, B. Cells showing atypic mitoses. C. Cells showing fusion of the protoplasm, formation of the so-called giant cells of cancer.

Technique: Tissue fixed in Heidenhain's corrosive sublimate solution, paraffin infiltration, hæmatoxylin, and Van Gieson. B. and L. 1/6 in. obj., 1 in. oc.

egg. Both the tumor and breast were movable, but there was axillary involvement. This proved so extensive that much of the growth could not be removed at the time of operation. It afterward grew rapidly, œdema and pain became intense, and the patient when last seen was sinking rapidly. The inner half of this tumor was given eight ten-minute exposures to the X-ray at intervals of two to three days. After the fifth treatment the exposed portion of the tumor became noticeably softer. Operation was performed March 29, 1902, by Dr. Da Costa,

the specimen received for examination being the entire breast and axillary glands. Palpation showed the exposed area to be distinctly softer than the remainder of the tumor, especially the lower end, where slight fluctuation could be detected. A needle prick into the breast just within the line separating the exposed from the unexposed areas was followed by the escape in jet of a fluid resembling serous pus. Incision of the exposed area showed surfaces studded with small, yellowish areas, apparently fatty in nature. This appearance gradually diminished toward the depth of the mass, except at the lower end, where there existed a partially filled cavity, 0.5 x 1.5 cm. in dimensions. This cavity approached closely to the skin at the point pricked

FIG. 2.



CASE I.—Scirrhous carcinoma. Section from exposed area. Field includes the contents of a large alveolus. Plasmatolysis and chromatolysis, which in parts of the section have terminated in the formation of a finely granular acidophilic detritus, are present throughout the field.

Technique: Tissue fixed in Heidenhain's corrosive sublimate solution, paraffin infiltration, hæmatoxylin, and Van Gieson. B. and L. 1/6 in. obj., 1 in. oc.

by the needle, and contained fluid resembling that evacuated by the puncture. The tissue surrounding this cavity showed the yellowish, fatty appearance to a marked degree. Microscopic examination of the fluid showed it to contain a moderate number of large cells, 12 to 16μ in diameter, having hyaline protoplasm and granular nuclei. Treatment with Sudan III. and osmic acid showed these cells to be practically filled with fat granules. In addition the fluid contained red and white (lymphocytes) blood corpuscles and granular débris.

Sections from the unexposed portion of the tumor (Fig. 1) show it to be a scirrhous carcinoma. In many portions of the sections are dense collections of lymphoid cells. A few polymorphonuclear leuco-

cytes and plasma cells are also seen. There are fairly numerous thick-walled bloodvessels, but very few of these show evidence of deposits on their inner surfaces. Staining by Gram's method shows the presence of a large number of small hyaline bodies resembling the so-called corpora amylacea. Mitotic cells are fairly numerous. Plimmer's bodies are present. No bacteria are demonstrable.

Sections from the exposed portion show the same general characteristics (broadly speaking), but the following differences are noted: 1. There are large areas of necrotic tissue, especially in those portions which border on the cavity described. (Fig. 2.) Some of the necrotic material is homogeneous in appearance, while other portions show the outlines of large cells, the protoplasm of which is in various stages of vacuolization and fragmentation, the nuclei having disappeared. Near the junction of these necrotic areas with the less conspicuously altered tumor are detached clusters of epithelial cells, the protoplasm of which has fused, the nuclei being in various stages of degeneration. The cells of the tumor bordering the necrotic area also show the changes just described, the degree of change becoming less as the distance from the necrosed area increases; but degenerative or necrotic changes in some degree are present in practically all the epithelial cells of this portion of the tumor, and distinct areas of beginning necrosis are scattered throughout. Special staining as well as the reactions to ordinary stains show that this degenerated material is not colloid in nature. 2. Collections of lymphoid cells are very few in number as compared with those in the unexposed portion. In the necrotic areas are a very few cells resembling polymorphonuclear leucocytes, but it is difficult to say whether they are such or are greatly changed epithelial cells with fragmented nuclei. My belief is that they are the latter. 3. Very few of the small hyaline bodies are present. 4. Some bloodvessels show endarteritis, deposits on the inner surface partially or almost wholly occluding them. 5. No mitoses are seen. Plimmer's bodies are not present in the most necrotic areas, but in other portions appear to be as numerous as in the unexposed areas. Elastic tissue is apparently more abundant than in the unexposed sections.

Case II.—W. N., aged fifty-seven years, patient of Dr. Sweet. Lymphangio-endothelioma of the orbit. The growth involved the nose and frontal sinus, and was making its appearance at the inner canthus of the opposite eye when the patient entered a distant hospital and was lost sight of. This tumor was not examined until after five ten-minute exposures to the X-ray, no tissue having been removed before treatment was begun. Sections of the tumor have for the most part a scanty fibrous tissue stroma inclosing alveoli lined with from one to several layers of large polymorphous endothelial cells. The alveoli contain masses of cells showing varying degrees of necrosis. In a few instances the outline of the cell is distinguishable, as is also the nucleus, the protoplasm being markedly vacuolated. The greater number of the cells do not show a distinct outline, the protoplasm being indistinct or irregular, or has even partially disappeared. The nuclei of these cells are fragmented, the fragments staining deeply with basic dyes. In some cells the process has gone still further, only a homogeneous material with no evidence of nuclei being present. In many of the alveoli the lining cells show the same beginning degeneration. Some of the larger necrotic areas have undoubtedly been formed

by the fusion of several alveoli, as in them fragments of degenerating trabeculæ are seen, more commonly near the periphery. Bloodvessels are fairly numerous and have very thin walls. No bacteria are demonstrable. Mast cells are present. Elastic tissue is very scanty. The necrotic changes in this tumor, though less advanced, are the counterpart of those found in Case I.

CASE III.—F. M., colored, aged fifty-two years, patient of Dr. Da Costa. Ulcerated area, 9 x 12 cm. in size, of one year's duration, on inner aspect of right knee, having developed in the scar of a burn received when the patient was eight years of age. Examination of a small bit of tissue removed showed it to be a typical squamous-cell epithelioma containing an unusually large number of keratinized areas, the so-called pearls. Collections of lymphoid cells were numerous. X-ray treatment was begun and twenty ten-minute exposures of about two days' interval given. Improvement was slow, and, excessive pain persisting, the leg was amputated. Examination of the removed tumor shows only a moderate change as a result of treatment. Collections of lymphoid cells are equally numerous. Bloodvessels show an increase of fibrous tissue, with fragmented inner elastic layer. The lumen of some is occluded. Epithelial cells in areas most free from pearls show varying degrees of necrosis, as vacuolization, fusing of protoplasm, and fragmentation of nuclei. These changes can scarcely be detected in areas composed mainly of pearls, which are very numerous. Elastic tissue is very abundant, apparently an increased amount over that found in sections from the tumor before exposure. Sections stained with toluidin blue and by Gram's method show cocci and bacilli of various sizes to be exceedingly numerous. Sections of the internal popliteal nerve underlying the tumor after being treated by Marchi's method show fatty degeneration and fragmentation of some of the -elin sheaths. These changes appear to be partly of recent origin and partly of longer duration. Bloodvessels of the nerve show endarteritis, the lumen of many of them being almost obliterated.

CASE IV.—R. B., aged thirty-two years, patient of Dr. Sweet. Large ulcerated surface on side of head, of ten years' duration. Growth extends posteriorly two inches behind the mastoid process and anteriorly to the orbital ridge, the ear being entirely gone. On August 7th a bit of tissue was removed for examination, which proved the growth to be a squamous epithelioma containing a few pearls. On August 14th treatment was begun. On August 29th a second piece of tissue was removed and examined, ten ten-minute exposures to the X-ray having been given. Though the clinical results were most satisfactory —cessation of profuse discharge, smoothing and healing of granulating surfaces, disappearance of pain—the microscopic changes are the least of any case examined. There is an increase of elastic tissue. In a few areas there is slight evidence of a beginning degeneration in the epithelial cells, but this is nowhere advanced. Infiltration of lymphocytes is about equal in the two specimens. Vessel walls show slight if any change. The report from this case, October 3d, is that healing still continues, but the portion of the growth from which the second specimen was removed shows the least progress. The affected area is so large that not all is exposed to the X-ray at each sitting. This probably accounts for the slight changes observed in the tissue after irradiation.

To summarize, the study of these cases shows: 1. Necrosis of cells and trabeculæ of varying degree. In Case I. there is also marked fatty degeneration. 2. Increase of elastic tissue in the three cases examined both before and after exposure. 3. Fewer areas of lymphocytic infiltration in one case after exposure, about equal numbers in the others. 4. A tendency to occlusion of vessels by deposits on their inner surfaces. This is marked in some instances, not so prominent in others. 5. Practically entire absence of infiltration by polymorphonuclear leucocytes.

Conclusions are hardly warranted by the results of these examinations, especially as further studies are being made with reference to nerve changes in irradiated tissue. Investigations regarding blood changes in persons undergoing this treatment and the tissue changes in normal rabbits that have been X-rayed are also under way. A few thoughts, however, suggest themselves:

1. Beck and others lay great stress on bloodvessel changes as the cause of necrosis. While endarteritis is probably induced by the X-ray, the accompanying tissue necrosis seems out of proportion to the vessel changes, suggesting the possibility of these being *pari passu* results of the same influence, instead of cause and effect.

2. The presence of immense numbers of cocci and bacilli in the tissues of Case III. after twenty exposures to the X-ray would argue against the possession by that agent of bactericidal power. It should be said that the pathogenicity of these organisms was not proven.

3. The unsatisfactory clinical results as well as the slight microscopic changes in Case III. can probably be safely attributed to the presence of the exceedingly numerous keratinized areas or "pearls." This emphasizes the importance of curetting or cutting away diseased tissue, whenever feasible, before instituting treatment by the X-ray.

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PARACOLON INFECTIONS, WITH REPORT OF THREE CASES.

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Within the past six years, and especially within the past few months, increasing attention has been drawn to a class of cases which clinically resemble typhoid fever, but which careful bacteriological examination has shown to be due to infection by organisms intermediate between the typhoid and colon bacilli.

For these organisms and the infection which they produce the terms "paratyphoid" and "paracolon" have both been used. Achard and Bensaude,[1] who reported the first cases, entitled them "paratyphoid infections." Widal and Nobecourt[2] opposed this term, and called their organism the paracolon bacillus, claiming that it more closely resembled the colon than the typhoid bacillus. Libman[3] suggests that for the present the term "paracolon" is the preferable one, and would reserve the name "paratyphoid" for those organisms which culturally are identical with the typhoid bacillus, but which are not agglutinated by typhoidal serum.

The earlier reported cases of paracolon infection have been so thoroughly and so recently reviewed that anything more than a brief mention of them seems unnecessary at this time. Achard and Bensaude, in 1896, reported two cases. The first case resembled typhoid fever, and was complicated by double femoral phlebitis and by cystitis or pyelonephritis. From the urine was isolated a paracolon bacillus. The second case was that of an infant which developed suppuration of a sternoclavicular articulation following a febrile attack of some two weeks' duration. The joint was opened, and from the pus was grown a bacillus identical with that obtained from the first case.

In 1897 Widal and Nobecourt isolated a paracolon bacillus from an abscess in the neck, near the œsophagus.

Gwyn,[4] in 1898, reported a case which clinically was typical of typhoid fever complicated by intestinal hemorrhage. From the blood he isolated a paracolon bacillus.

Cushing,[5] in 1900, isolated a paracolon bacillus from a costochondral abscess. His patient had nine months previously suffered from an illness, with relapse, supposed to have been typhoid fever.

In 1900 Schottmüller[6] reported one case, and the following year six additional cases. In all but the last case he isolated paracolon bacilli from the blood; the serum of the seventh case agglutiuated the bacilli from certain of the other patients.

In 1901 Kurth[7] reported five cases which he considered examples of paracolon infection. From the urine of one patient and the feces of another he isolated bacilli which were agglutinated in high dilutions by the serum of four of the cases. The serum of the fifth case—the one with bacilli in the urine—was not tested.

In April of this year Brion and Kayser[8] reported a case of infection resembling typhoid, complicated by relapse and thrombosis of the left leg. A paracolon bacillus was isolated from the blood, urine, feces, vagina, and rose-spots.

In May, 1902, Strong[9] reported an autopsy done forty-two hours after death on a patient who was supposed to have died from typhoid fever. From the spleen was obtained a paracolon bacillus. No lesions were found in the intestinal tract.

In June, 1902, Buxton and Coleman[10] reported a case resembling typhoid fever from whose blood was isolated a paracolon bacillus.

In the same month Berg and Libman[11] reported an interesting case of typhoid fever with a secondary infection with a paracolon bacillus. The clinical picture was that of cholecystitis, and during life the paracolon bacillus was isolated from the gall-bladder, blood, and urine. No typhoid bacilli were cultivated, but the patient's serum agglutinated typhoid bacilli at dilutions of 1 : 250, besides giving a reaction with the paracolon bacillus. At autopsy healing ulcers were found in the ileum.

Hume[12] has recently reported a case typical of typhoid fever, with relapse, intestinal hemorrhage, and cystitis. A paracolon bacillus was isolated from the urine and feces.

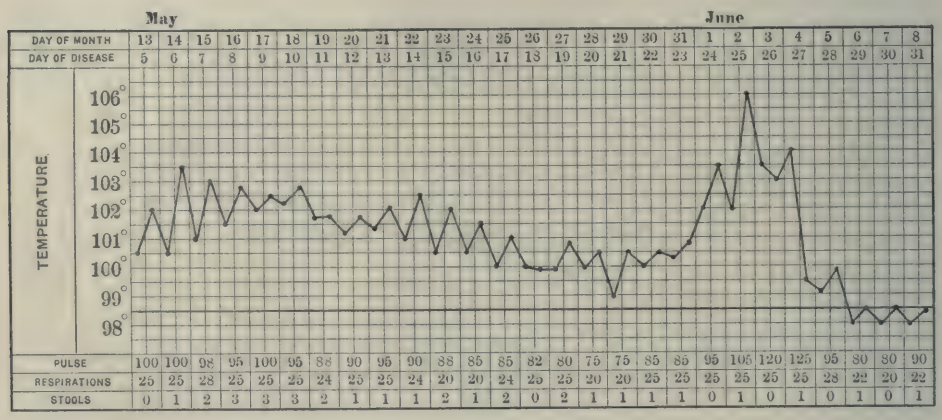
The last cases, seven in number, are reported in August of this year. Johnston[13] presents four, in two of which paracolon bacilli were isolated from the blood. In the other two the diagnosis was made on the strength of the serum reactions. There were no complications. Hewlett[14] reports one with isolation of the bacillus from the blood. His patient had a relapse complicated with bronchopneumonia. Longcope[15] reports two cases, with isolation of the bacilli from the blood in both instances. His second case had a relapse. The first case was very

severe, and proved fatal on the twelfth day of the disease. At autopsy the intestinal tract was found practically normal. This is the first complete autopsy report on a case of pure paracolon infection.

To this list I desire to add the reports of three cases recently observed at Lakeside Hospital. All occurred in the service of Dr. E. F. Cushing. The first case is to be reported later from the surgical side. Dr. G. W. Crile has kindly allowed me to use the surgical records to complete the history.

CASE I. *Paracolon infection; mild course; suppurative cholecystitis during convalescence; incision and drainage of gall-bladder; paracolon bacilli in pus; right lobar pneumonia; recovery.*—M. S., white, male, aged thirty years. Admitted May 13, 1902, complaining of headache, vomiting, loss of appetite, and general weakness. Family and past history unimportant. The present illness began four days before admission, though for two weeks past he had felt weak and drowsy, and had lost his appetite. The initial symptoms were headache, general soreness, slight cough without expectoration, and persistent vomiting. For the past four days he had vomited practically everything taken. Took to bed May 10th.

CHART I.



On examination the patient was well nourished; slightly anæmic. The tongue was dry, coated, and tremulous. Pulse slightly dicrotic. Heart and lungs negative. Liver dulness in the mammillary line extended from the fifth rib to a point two fingers' breadth below the costal margin, where the edge was distinctly felt. The abdomen was full, tympanitic, not tender. The spleen was readily palpated. There were no visible rose-spots. Temperature, 100.5° F.; pulse, 105; respirations, 25. The urine was high colored, acid, specific gravity 1025; no sugar; trace of albumin; an occasional hyaline cast and a few leucocytes. No diazo reaction.

May 14th. Widal reaction negative. No tubercle bacilli in the sputum.

From admission until May 30th the course of the disease was mild and uneventful. The highest temperature was 103.8° F.; it fell slowly and touched normal for the first time on May 29th. On May 18th the patient's serum was tested with a paracolon bacillus, but the result

was negative. On May 25th the Widal reaction was again negative. No rose-spots were ever found. The leucocyte count continued normal. In spite of the negative Widal reaction the case was considered to be a mild typhoid.

29*th*. In the evening the patient had an attack of slight abdominal pain associated with nausea and vomiting. Examination of the abdomen was negative, and the pain soon subsided.

30*th*. In the afternoon the patient again complained of abdominal pain, which he described as cramp-like and felt rather generally over the upper right half of the abdomen. The muscles over the right half of the abdomen were held slightly more rigid than over the left, and there was little tenderness on deep pressure in the right half of the umbilical region. Temperature, 100° F.; pulse, 88; respirations, 25. Leucocytes, 12,000.

31*st*. Still slight abdominal pain; nothing additional made out on examination. Lungs and heart negative. Temperature, pulse, and respirations practically unchanged. Leucocytes, 12,000.

June 1*st*. Abdominal pain still complained of, and is now located in the right hypochondrium. There is increased muscular resistance over the right half of the abdomen and decided tenderness in the region of the gall-bladder, which can now be felt as a rounded mass extending to a point 4½ cm. below the costal margin. Temperature at 8 A.M., 102° F.; pulse, 90; respirations, 25. At 8 P.M. temperature, 103.2° F.; pulse, 100; respirations, 28. Leucocytes, 10,000. No bile in the urine; no jaundice.

2*d*. The patient had a comfortable night, and this morning feels much better; abdominal pain almost gone. Examination of the abdomen shows less muscle rigidity and decidedly less tenderness, but the gall-bladder is still palpable and quite sensitive. No jaundice; no bile in the urine. Temperature, 102° F.; pulse, 100; respirations, 25. Leucocytes, 13,000. The question of operation was discussed, but it was decided to await further developments. No change was noticed until 2 P.M., when there was a return of the abdominal pain, and the patient vomited. This was repeated at 3 P.M. At 4 P.M. the patient had a hard, shaking chill, lasting ten minutes, and the temperature rose to 106° F. Aside from increased tenderness over the gall-bladder the abdominal examination remained the same. Leucocytes, 15,800.

Immediate operation was decided upon, and was performed by Dr. G. W. Crile. Cocaine anæsthesia was used. The gall-bladder was found distended and adherent to the parietal peritoneum. On incising it there escaped several ounces of a turbid fluid, which was followed by a small amount of pus. No calculi were found. The gall-bladder was drained and the wound closed. Cultures from the fluid yielded a pure growth of an actively motile bacillus with the characteristics to be described later.

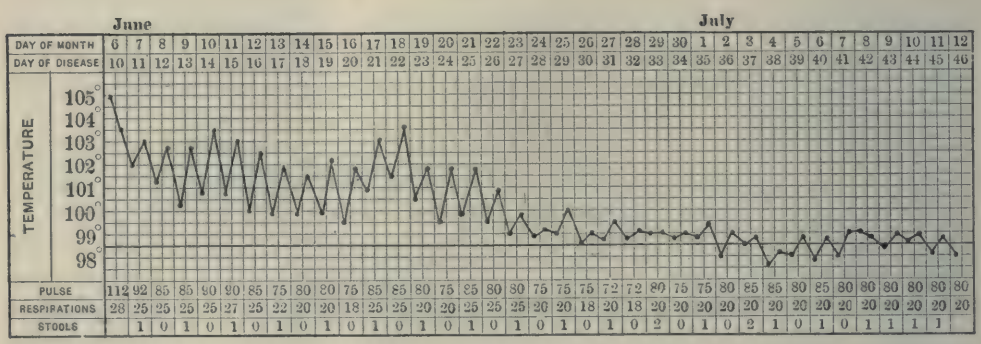
The following day, June 3d, the temperature continued elevated, and the patient complained of cough and expectoration. Examination of the lungs showed a consolidation of the lower right lobe. The next day, June 4th, the temperature fell by crisis, and thereafter continued normal throughout the patient's stay in the hospital. The lung signs cleared up rapidly.

The patient convalesced uninterruptedly, and was discharged July 6th, a very small fistula still remaining at the site of the operation.

Case II. *Paracolon infection; mild course; cystitis on seventeenth day; thrombosis of left femoral vein on twenty-first day; paracolon bacilli from blood and urine; recovery.*—M. E., male, Australian, aged twenty-six years. Admitted June 6, 1902, complaining of headache, fever, and loss of appetite. Family and past history are unimportant. Present illness began about two weeks ago, with headache, slight cough, and coryza. For a few days had mild diarrhœa; since then has been constipated. Appetite gradually failed, and there has been rapid loss of strength. No nausea or vomiting; no chilliness; no epistaxis. Took to bed the day before admission.

Physical examination showed a well-nourished man looking decidedly ill. Expression dull; face flushed; tongue moist, coated, and tremulous. Pulse of good volume; slightly dicrotic. Lungs negative. Systolic murmur at the apex of the heart; normal area of dulness. Abdomen soft, not tender. Spleen readily palpable. No rose-spots. Liver dulness extended 4 cm. below the costal margin in the mammillary line; edge palpable. Some reddening, swelling, and tenderness about the left ankle-joint, due to a recent injury. Temperature, 105° F.; pulse, 112; respirations, 28. The urine was clear, acid,

Chart II.



specific gravity 1019; no sugar; very faint trace of albumin; no diazo reaction; microscopically contained a few coarsely granular casts.

After admission until June 16th the course of the disease was fairly typical of mild typhoid fever. The temperature was slightly irregular, ranging from 100° to 104° F. The pulse was slow, averaging 85 per minute. A few rose-spots were noted, and the spleen was always readily palpable. The leucocytes ranged from 6000 to 9000. The bowels were constipated, requiring enemata. For the first three days it was necessary to catheterize the patient; subsequently he voided urine without difficulty. The Widal reaction, tested frequently, was never positive at dilutions greater than 1 to 10. A blood culture taken June 7th yielded an actively motile bacillus, which will be described below.

On June 16th the patient first noticed slight pain in the left groin, but made no complaint until two days later. Examination at that time disclosed slight swelling of the whole left leg. The foot appeared congested, and there was marked prominence of the superficial veins of the calf and thigh. The surface temperature was not altered. On palpation there was tenderness along the course of the femoral vein and in the popliteal space. The temperature was 103.5° F., which was

about 2° higher than it had been running. The leucocyte count was 9000.

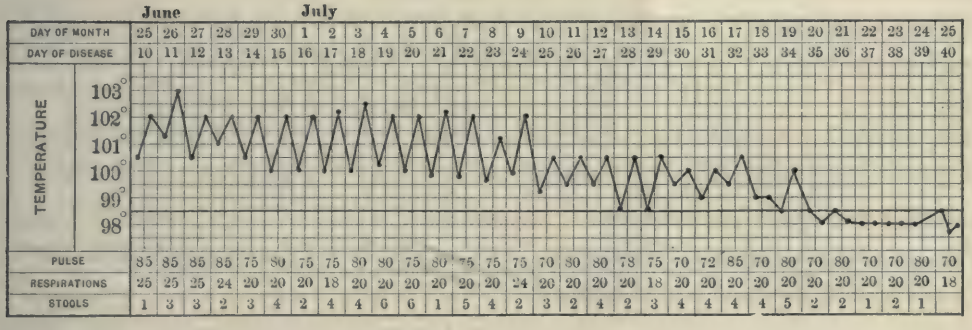
Two days later, on June 20th, a definite cord-like thickening could be made out in the upper part of the thigh over the situation of the femoral vein. This was decidedly tender on palpation. Nothing was to be felt in the popliteal space.

On June 13th pus cells were noted in the urine, and on June 21st a culture yielded a large number of colonies of a bacillus identical with that isolated from the blood; also a few colonies of a streptococcus.

The subsequent course of the disease was uneventful. The temperature reached normal on June 29th, and there was no subsequent rise. The tenderness in the left leg persisted for a few days. The leg never regained its natural size, and the superficial veins remained prominent. Under treatment with urotropin the urine cleared rapidly, and at the time of discharge contained very few pus cells, and no paracolon bacilli could be found on culture. The patient was discharged on July 12th.

Case III. *Paracolon infection; mild course without complications; recovery.*—D. L., male, white, aged thirty-five years. Admitted June 25, 1902, complaining of fever, loss of appetite, and diarrhœa. Family

Chart III.



and past history are unimportant. For the past four weeks patient has not done any work on account of weakness and loss of appetite. On June 16th had a shaking chill, followed by fever and headache. No subsequent chills; no epistaxis. The bowels have been loose for a week previous to admission. The patient has remaind in bed since June 16th.

Physical examination disclosed a fairly well-nourished man; slightly anæmic. Tongue moist, coated, and fissured. Pulse regular, and not dicrotic. Heart and lungs negative. Abdomen held rather rigidly; no tenderness. Border of spleen palpable; a few scattered rose-spots; normal hepatic dulness. Temperature, 100.5° F.; pulse, 90; respirations, 25. Urine clear, acid, specific gravity 1015; no sugar or albumin; microscopically a few leucocytes and an occasional hyaline cast. Diazo reaction positive. Leucocytes, 4400. The Widal reaction, tested on June 29th, July 2d, 11th, and 26th, was persistently negative at dilutions of 1 : 50, though a positive reaction was sometimes obtained at 1 : 10. On July 2d and 11th the patient's serum

gave a positive reaction with the organisms obtained from the first two cases at a dilution of 1 : 50.

The course of the disease was that of a mild typhoid fever without complications. The temperature never rose above 103.5° F. It reached normal July 19th. The bowels were loose throughout the early stage of the illness. Convalescence was rapid and uneventful, and the patient was discharged July 26th. A blood culture on June 29th, the fourteenth day of disease, remained sterile. A urine culture taken during convalescence was negative for paracolon bacilli.

Bacteriology. The organisms obtained from the first two cases were practically identical, and one description will answer for both. They were very actively motile organisms, having the morphology and staining properties of B. typhosus. The growth on agar and in gelatin was similar to that of B. typhosus. Bouillon was diffusely clouded; no surface pellicle was formed after ten days' incubation. A slight trace of indol was formed in Dunham's peptone medium after one week.

On potato there was a barely perceptible growth appearing as an increase of the moisture along the line of stroke. Litmus milk was slightly acidified after twelve hours; after one week there was distinct reduction of the acidity, and by ten days the color equalled that of the control. After two weeks there was distinct alkali production. The organism from Case I. ("Samuels") produced slightly more alkali that that from Case II. ("Euster"). There was no coagulation of the milk after four weeks' incubation. Both organisms fermented glucose and maltose, with the production of acid and visible gas, but did not ferment lactose or saccharose. No animal experiments were performed. The organisms agree, therefore, very closely with most of the paracolon bacilli heretofore described.

Agglutination Tests. In all the tests a time limit of one hour was used, and a reaction was not called positive unless there was good clumping and cessation of all motility. In none of the cases was a positive Widal reaction obtained in dilutions greater than 1 : 10, though tests were made frequently throughout the course of the disease. The serum from Samuels, Case I., agglutinated B. "Samuels" and B. "Euster" in dilutions of 1 : 100; likewise the serum from Euster, Case II., agglutinated B. "Samuels" and B. "Euster" in dilutions of 1 : 200. The serum from Lawton, Case III., agglutinated B. "Samuels" and B. "Euster" in dilutions of 1 : 50. In addition, the sera of Cases I. and II. were tested with Gwyn's paracolon bacillus and one of Johnston's organisms, and in both instances gave positive reactions in dilutions of 1 : 50. B. "Samuels" and B. "Euster" were tested with several different typhoid sera of high agglutinative strength, but without any reaction in dilutions of 1 : 10.

The following table may assist in making these reactions clear:

Serum.	Organism.	1–10	1–50	1–100	1–200
Samuels. Case I.	Samuels	+	+	+	—
	Euster	+	+	+	—
	Gwyn	+	+	0	0
	Johnston	+	+	0	0
	B. typhosus	+	—	—	0
Euster. Case II.	Samuels	+	+	+	+
	Euster	+	+	+	+
	Gwyn	+	+	?	0
	Johnston	+	+	+	0
	B. typhosus	+	—	—	—
Lawton. Case III.	Samuels	+	+	0	0
	Euster	+	+	0	0
	B. typhus	+	—	0	0
Typhoid, agglutinative strength 1–200	Samuels	—	—	0	0
	Euster	—	—	0	0

0 = no test made. ? = doubtful reaction.

Johnston in his recent article has analyzed all the reported instances of paracolon infection. Most of the cases have run a course fairly typical of comparatively mild typhoid fever, and without the aid of the serum reaction or a bacteriological examination a differential diagnosis would be impossible. Rose-spots and a palpable spleen have been present in a majority of instances. Relapse has been comparatively common—at least five cases. Both of Longcope's cases are unusual in that labial herpes was present. The onset of one of his cases was with a chill. Our third case gave a similar history. The very wide distribution of the bacilli in the body is indicated by Brion and Kayser's case.

Many of the common and several of the uncommon complications of typhoid fever have occurred. Of the former there have been reported intestinal hemorrhage, cystitis, femoral phlebitis, furunculosis, and bronchopneumonia; of the latter suppurative arthritis, myositis, osteomyelitis, and suppurative cholecystitis.

Our first case is especially interesting as being the first recorded instance of suppurative cholecystitis complicating a paracolon infection. The clinical picture of Libman's case resembled cholecystitis, but at operation the gall-bladder was distended with dark, thick bile, and at autopsy the bladder wall showed no change. Cholecystitis, both suppurative and non-suppurative, is of course a well-recognized complication of typhoid fever, and its occurrence in a paracolon infection serves to again emphasize the marked similarity of the clinical picture of the two diseases. The ease of performance and the success of early operation in this complication is also well shown in this case.

Longcope in his paper discusses the pathology of the disease. There have been three fatal cases, with autopsies in each instance. Berg

and Libman's case was a mixed infection, probably primarily typhoid fever, with a secondary infection with the paracolon bacillus. Healing ulcers were found in the ileum. In Strong's case no clinical history is available. The autopsy was done forty-two hours after death, and Strong himself suggests that the bacillus isolated from the spleen may possibly have been a post-mortem invader. The large and small intestines were normal throughout. The mesenteric lymph glands were enlarged, and a few were hemorrhagic. Fresh smears from the spleen showed a few crescentic æstivo-autumnal malarial parasites and some pigment; but it seems unlikely that the patient's death was due to malaria. He had been treated with quinine.

Longcope's case is complete. Autopsy revealed only the lesions of an acute infection—acute splenic tumor, cloudy swelling of the liver and kidneys, focal necroses in the liver. The mesenteric lymph glands were not swollen, and both large and small intestine were practically normal.

While no very definite conclusion can be drawn as yet regarding the pathology of the disease, it is evident that we are dealing with an infection quite distinct from typhoid fever. That all of the cases of apparently pure paracolon infection may not, however, be as simple as Longcope's case might lead us to suppose is suggested by the occurrence in two instances of well-marked intestinal hemorrhages.

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MALTA FEVER: ITS OCCURRENCE IN THE UNITED STATES ARMY, WITH A REVIEW OF THE LITERATURE.[1]

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Historical. Medical officers of the English army were the first to draw attention to a disease prevailing in Malta and other Mediterranean stations possessing many of the symptoms of typhoid, but differing from that disease in important respects.

In 1816 Burnett[2] described very fully this disease, but regarded it as being a remittent malarial fever. This view of the character of the fever was adhered to for many years, and it was not until 1878 that the distinction was clearly drawn by medical officers of England between remittent malarial fever and Malta fever.

When first described the disease was supposed to be peculiar to the Island of Malta, hence the name "Malta fever;" but continued observation has proven that it is a widespread disease throughout tropical and subtropical regions. Thus Donaldson[3] has described cases in Gibraltar, Tomaselli in Sicily, Patterson in Constantinople, Oliver[4] along the banks of the Danube, Veale[5] in Cyprus, Musser[6] and Cox[7] in Porto Rico, and Chamberlain,[8] Curry,[9] and Strong[10] in the Philippines.

Many and various were the opinions held by observers as to the etiological factors in the production of Malta fever, and it was not until the painstaking researches of Bruce were published in 1887 that anything positive was known as to the etiology. Bruce[11] demonstrated the cause of the disease to be a micrococcus, to which he gave the name "micrococcus melitensis." His researches threw a flood of light upon the etiology and pathology of this hitherto obscure disease.

I shall not enter here into any detailed description of the pathology or symptomatology of Malta fever, save to say that it is generally a fever of long duration, subject to frequent relapses, presenting a most irregu-

[1] With permission of the Surgeon-General, U. S. A., from report to the Surgeon-General.
[2] Burnett. Practical Account of the Mediterranean Fever, London, 1816.
[3] Donaldson. Army Statistical Reports, 1839.
[4] Oliver on Danubian Fever. Lancet, 1892, vol. ii. p. 1359.
[5] Veale. Report on Cases of Fever from Cyprus, Malta, and Gibraltar. Army Medical Department Reports, England, 1879.
[6] Musser. Philadelphia Medical Journal, December, 1898.
[7] Cox. Report of Surgeon-General, U. S. A., 1899, p. 285.
[8] Chamberlain. Report of Surgeon-General, U. S. A., 1900, p. 226.
[9] Curry. Report of Surgeon-General, U. S. A., 1900, p. 226; also Journal of Medical Research, July, 1901, vol. vi. No. 1, pp. 241–248.
[10] Strong's Report of the Surgeon-General, U. S. A., 1900, p. 227.
[11] Note on Discussion of Micro-organism in Malta Fever, Practitioner, vol. xxxiv. p. 161; also Observations on Malta Fever, British Medical Journal, May 18, 1889.

lar and confusing temperature course and accompanied by severe pain in the joints, constipation, profuse perspiration, and often followed by arthritic pains, with or without swelling of the joints. An enlarged and tender spleen is very common. The diagnosis of the disease has heretofore presented many difficulties, as it resembles in many instances typhoid or remittent malarial fever; and even with the help of the microscopic examination of the blood and the Widal test the distinction between these diseases cannot always be made. In 1897, however, Wright, of the Royal Army Medical School, England, discovered that the blood serum of a patient suffering from Malta fever will agglutinate the micrococcus melitensis in very dilute solution, and that this agglutination test is most delicate and can be depended upon absolutely in diagnosis. I will give in detail the methods of performing the test later.

Description of Cases. At the United States Army General Hospital, Presidio of San Francisco, Cal., the blood of every patient admitted is examined microscopically, by order of Colonel Girard, the commanding officer. Unless specially requested by the attending surgeon, the Widal test and the agglutination test for Malta fever are not performed, so that it is possible, and indeed probable, that cases of Malta fever may have passed through the hospital without being discovered. By the courtesy of Professor Welch, Johns Hopkins University, and Professor Ophüls, Cooper Medical College, San Francisco, I have been supplied with cultures of the micrococcus melitensis, and these have been used in making the agglutination tests in the cases about to be reported.

From December 1, 1901, to date (March 24, 1902) four cases of Malta fever have come under my observation at this hospital—two during acute exacerbations of the disease and two during the chronic stage.

Case I. *Two attacks of Malta fever, the first complicated by combined æstivo-autumnal and tertian malaria.*—This case occurred in the person of an assistant in my laboratory, who had suffered repeatedly from attacks of malarial fever, and was under the medical care of Dr. Edmund Barry, to whom I am indebted for the clinical data.

History of the Case before Admission. Name, Gustav T. W. S., private, Hospital Corps; aged twenty-eight years; birthplace, Germany. Enlisted in the United States army April 7, 1898, in New York city. He arrived in New York city from Europe in 1891, and had never been sick prior to enlistment. After enlistment he was immediately ordered to Tybee Island, Ga., where he joined Battery "F," Fifth United States Artillery. He left Tybee Island with the Battery, April 23, 1898, and was next stationed at Chickamauga Park, Tenn., where he remained one week, at the end of which time he went to Fort Tampa, Fla., and about July 1st arrived at Santiago de Cuba. He had not been sick up to this time. After the surrender of Santiago he camped until about August 15, 1898, near El Caney, and while in this camp often had slight chills, followed by a rise of temperature, and was treated with quinine. Before embarking for the United States he was stationed

for one week in the city of Santiago, doing guard duty in the streets, where he had too sleep. He left, August 23d, for the United States, and went on sick report the next day, the physician diagnosing the fever from which he was then suffering as typhoid. On September 1st he arrived at Montauk Point, Long Island, where he stayed for five days, when he was transferred to St. Catherine's Hospital, Brooklyn, N. Y. Here he improved rapidly, and about September 16, 1898, was taken as a convalescent to Shepley Hall, Atlantic Highlands, N. J., through the kindness of Miss Helen Gould. About October 4, 1898, he was granted a furlough for one month to visit Brooklyn, N. Y. The next day he was seized with a severe chill, followed by high temperature, and sent by ambulance to the Methodist Episcopal Hospital, Brooklyn, where he stayed for two weeks, after which he was transferred to St. Catherine's Hospital. At this hospital his case was diagnosed as "typhoid malaria." About December 4, 1898, he reported for duty with his Battery at Fort Hamilton, N. Y., where he stayed until March 31, 1899. During this time he had several attacks of malaria, having chills followed by fever, nausea, and vomiting, pains in all the bones, and severe headache. On April 1, 1899, he left for Manila, by way of San Francisco, and was well until July of that year, when he had slight chills at San Pedro, Macati, P. I. He also suffered from attacks during August, 1899. During January, 1890, at Bacour, P. I., he had fever and chills, with severe pains repeatedly in all the joints. He was then transferred to Manila, and while on duty at the Medical Supply Depot in that city he had several attacks of fever, with pain in all the joints, severe headache, and high temperature. In November, 1900, he was ordered to the United States, his case being diagnosed as malarial cachexia, although he had never had an examination of the blood. From November, 1900, until September, 1901, he had several chills, followed by a rise of temperature, with pain in all the bones and in the lumbar region. At this time I discovered numerous æstivo-autumnal parasites in the blood.

History of the First Attack Complicated by Malaria. On September 4, 1901, the patient had a chill, and was admitted to the hospital. At this time an examination of the blood showed a few nearly full-grown tertian parasites and numerous æstivo-autumnal parasites. Patient appeared in fairly good condition, although somewhat anæmic. He presented a coated tongue, and complained of constipation, severe headache, and backache. Physical signs negative. The case at this time was supposed to be one of malarial fever, and quinine was given in large doses. The temperature at this time did not go above 102° F., and the treatment with quinine brought it down to normal in a few days, and the patient was returned to duty. On September 18th the patient had another chill, and was again put upon sick report. An examination of the blood at this time showed a few æstivo-autumnal parasites, and treatment with quinine was resumed. Patient complained of the same symptoms as in the previous attack, but mostly of severe pains in the joints. An examination of the blood was made every day, and the æstivo-autumnal parasites disappeared by the 21st, but the patient continued to run an irregular temperature. This irregularity continued, as will be seen by reference to the chart (Chart I.), until October 13th, during which time no malarial parasites could be demonstrated in the blood, and an examination was asked for as to

the possible occurrence of Malta fever. This examination was unsatisfactory because of the fact that my culture of the micrococcus melitensis had become infected, and it was impossible to secure a new one, It was noticed, however, that a partial agglutination was obtained. and from the history of the second attack I have no hesitancy in asserting that this continuation of the temperature after heroic doses of quinine was due to the presence of Malta fever. On reference to the chart it will be seen that the temperature shows a marked quotidian character, there being a daily rise and fall, much resembling that found in many cases of tuberculosis. The highest point reached at any time was 104° F., but most of the time the temperature did not go above 102° F.

The patient gradually convalesced, and was discharged from the hospital on October 19th, after a week's normal temperature. The symptoms complained of during the time in which the malarial parasites were absent from the blood were those of pain in the joints, a feeling of marked malaise, and considerable frontal headache. Patient appeared anæmic, the skin of a yellowish hue, and he became considerably emaciated. At this time he also suffered from a slight nephritis, as shown by an examination of the urine.

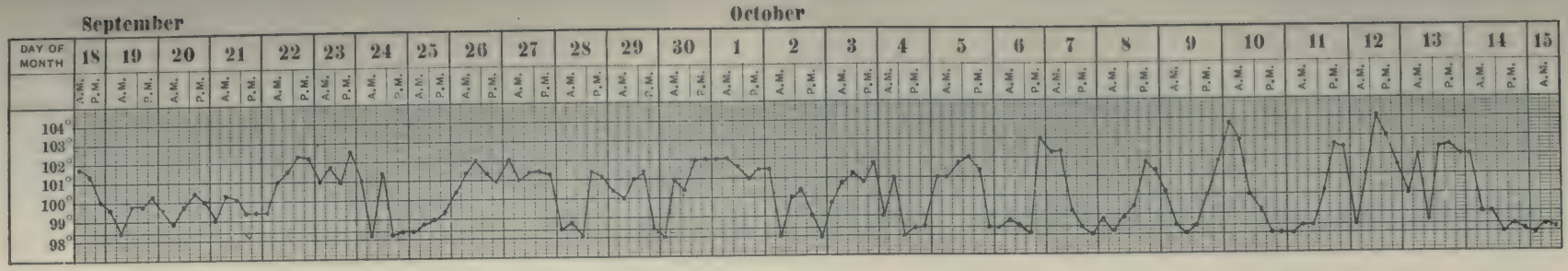
There can be no doubt, I believe, that this attack was due to Malta fever, but was complicated at its commencement by malarial fever, which soon succumbed to the influence of quinine, but which in no way affected the course of the Malta fever.

History of Second Attack. From October 19th to December 15th the patient remained comparatively well, although he complained at times of slight headache and chilly sensations, together with some pain, especially noticeable in the articulations. On the 15th of December he had a slight chill, and was readmitted to the hospital with a temperature of 100° F. An examination of his blood for ten consecutive days showed no evidence of malarial infection; but from the previous history of the case it was supposed that the temperature at this time was due to malaria, and large doses of quinine were administered. A request was not made for the Malta fever reaction until January 18th, at which time the temperature had reached normal. At this time the reaction was positive at once in a dilution as high as 1 to 250. This reaction was repeated several times, and was always found positive, and immediately cleared up the doubt which had attended the case from the commencement of the first attack.

The symptoms complained of during the second attack were similar to those of the first, there being marked pain in the joints, considerable headache, a furred tongue, and a markedly anæmic countenance. From a consideration of the chart of the second attack (Chart II.) it will be seen that the temper ature during this attack differed greatly from that of the first. During the first attack the temperature was markedly quotidian in character, while during the second the temperature stayed above normal for from five to seven days at a time.

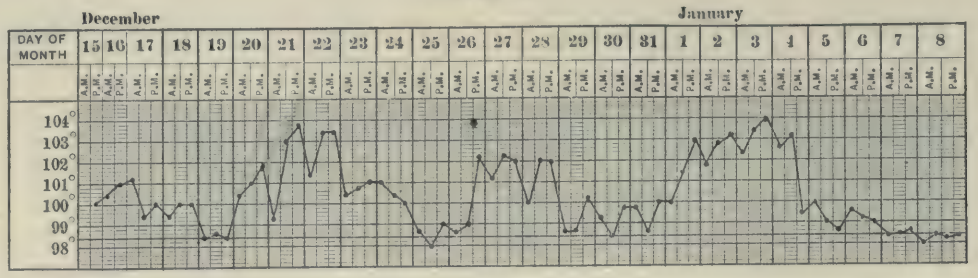
These two charts illustrate remarkably well the irregularities of the temperature in Malta fever during different attacks of the disease and of how comparatively little value the temperature chart is in these cases.

CHART I.



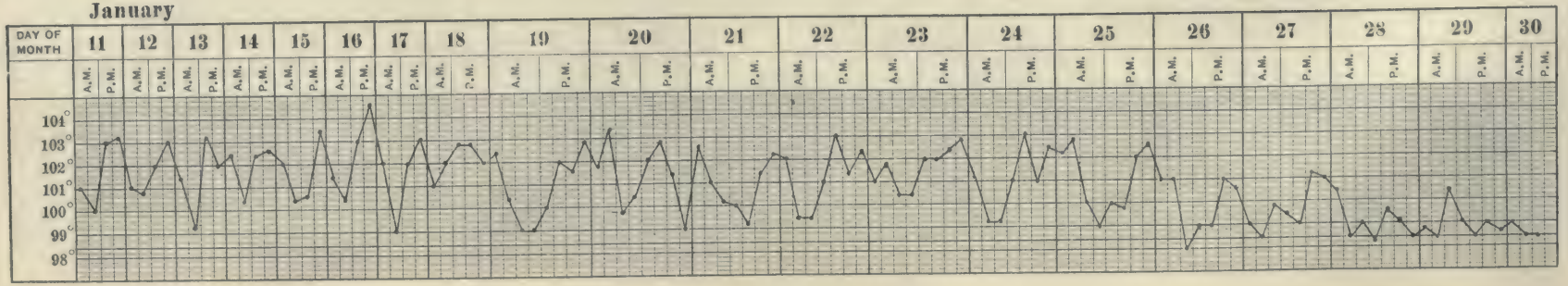
CASE I.

CHART II.



CASE I.

CHART III.



CASE II.

During the second attack the patient had no signs of nephritis, and this attack was not as severe or as long continued as the first. Patient was discharged from the hospital on January 19, 1902, having had a normal temperature for two weeks. Since that time there has been no repetition of the attacks, but he has complained considerably of stiffness in the joints and slight chilly sensations.

There can be no doubt but that this infection was contracted prior to the patient's arrival at this hospital, as he gives a distinct history of similar attacks in the Philippines, which were considered, however, of malarial character, the blood never having been examined. The occurrence of malaria, together with the first attack, further obscured the case, and led naturally to the inference that these attacks of fever were, in fact, due to malarial infection. This case shows the importance of blood examinations and the use of the agglutination test for Malta fever in the obscure fevers which are prevalent in the Orient.

Case II.—C. H. M., musician, Company "D," Twenty-seventh Infantry, aged twenty-three years; American.

History Previous to Admission. Patient gave but little history previous to admission save that of suffering from malaria in the Philippines. He had several attacks of slight chills, followed by fever, general pain, and severe headache while campaigning, and was diagnosed as a case of malarial cachexia. He was on sick report four or five days before admission to this hospital at the Presidio, complaining of pains in the left hypochondriac region.

History after Admission. On admission patient complained of severe pain in the lumbar muscles, tenderness upon pressure over the spleen, and headache. There was considerable cough present. Bowels were constipated, and there were some mucous râles heard at the base of the right lung. The patient had an irregular temperature previous to admission, and on January 7th had a distinct chill, the temperature reaching 103° F. An examination of the blood was negative for malaria. From this time the temperature stayed above normal until January 17th, as will be seen on referring to the chart (Chart III.). On the 14th a Widal test was requested, which was negative. At this time the temperature resembled that of typhoid fever very closely, although the patient had no symptoms referable to that disease, complaining mostly of pain in the back and slight headache. Upon the 16th of January a request was made for a Malta fever test, and a reaction was obtained almost immediately with a dilution of 1 : 100. This test was performed repeatedly afterward until the patient's discharge from the hospital, and was always positive. Upon referring to the temperature chart in this case it will be seen that the temperature curve is irregular, the temperature from January 7th to the 17th staying above normal and resembling that of typhoid; while after the latter date the temperature became more irregular, there being a daily remission, thus approaching the quotidian character shown in Chart I. The patient ran a temperature from January 7th until January 31st, and was then returned to duty after the temperature had remained normal for several days. This infection was undoubtedly contracted in the Philippines,

as the patient had been entirely well until his arrival in the islands, and there suffered from attacks which he said were similar to the present one. The chief symptoms complained of were muscular pain, especially prominent around the articulations, and slight headache. Bowels were constipated, and considerable anæmia developed during the attack.

Case III.—J. M., sergeant, Fourth Infantry, aged twenty-four years; American. The history of this patient previous to admission to the hospital was that of slight malarial attacks in the Philippines. On conversation with the patient he said he had suffered from several so-called malarial attacks in the Philippines, lasting from one to three weeks, although they were treated vigorously with quinine. There can be no doubt that these attacks were not malarial in character, and were probably due to Malta fever.

Upon admission to the hospital the patient appeared in good flesh, but was somwhat anæmic. He complained of constipation, there having been no bowel movements for several days. Besides constipation there was some tenderness in the region of the gall-bladder, and the patient said that he had suffered severely from muscular pain in the lumbar region and pain in the joints. Physical signs negative. Patient was admitted to the hospital January 21st, and complained of constipation. At the time of admission the temperature was 102° F., but an examination of the blood did not show any malarial infection. On January 24th a request was made for a Malta fever test, and an immediate reaction was obtained, very marked, with a dilution of 1 to 100. This reaction was repeatedly confirmed during the patient's stay in the hospital. From January 21st to the 29th the patient ran a low temperature, never above 102° F., and generally between 101° F. and normal. He complained mostly of pain in the joints. The tongue appeared fairly clean. There were no physical signs whatever which could be considered characteristic. On February 5th the patient was discharged from the hospital, having had a normal temperature since January 29th. I have not reproduced the temperature chart in this case, as it is uninteresting, showing simply a low quotidian temperature curve entirely uncharacteristic. The case is of value, however, in showing the unreliability of the temperature chart in Malta fever.

Case IV.—N. S. L., artificer, Fourth Infantry, aged twenty-three years; American.

History Previous to Admission. Patient suffered from repeated attacks of so-called malaria in the Philippines, having chills, severe muscular pain, and headache, these attacks lasting from one to two weeks. Patient's blood was never examined, but the attacks simulated those of malaria so closely that they were considered to be of that character. Quinine was given in large doses, but had no effect on the fever.

History after Admission. Patient was admitted to this hospital January 24, 1902, with a temperature of 103° F., and complained of severe headache, backache, and pain over the spleen upon pressure. There was a history of a decided chill. He appeared anæmic and jaundiced, and was constipated, and said that he had had similar attacks in the Philippines. An examination of the blood on the 25th was negative for malaria, but gave a marked reaction with the micrococcus melitensis in a dilution of 1:100. Patient's temperature reached normal on the 26th, although no quinine had been given, and remained normal

until February 4th, at which time the patient had a slight chill, the temperature reaching 103° F., and showing a quotidian character for a period of five days after. It remained normal until he was discharged, on the 19th. During this time the patient did not appear to be very sick, the only thing complained of being pains in the joints. The temperature chart is not reproduced, as it is not of special interest.

In considering the four cases noted it will be seen that the first two cases are those of acute exacerbations of Malta fever, in which the patient runs a temperature for a considerable length of time, while the latter two cases are characteristic of the chronic form of the disease, in which the temperature is but little above normal, and the chief symptoms present are those of articular rheumatism. Both of the latter cases would have been diagnosed as cases of articular rheumatism had it not been for the Malta fever reaction.

Methods of Performing Serum Tests for Malta Fever. The serum test for Malta fever was first described by Wright, of the Royal Army Medical School, at Netley. The methods of performing the test vary somewhat, but the principle is the same in all. He discovered that the serum of Malta fever cases had the power of agglutinating the micrococcus in suspension, and that this reaction took place earlier than the Widal reaction and in much more dilute solution.

Wright's Method. Sedimentation tubes having a diameter of less than 1 millimetre and an agar culture of the micrococcus are used in making the test. A salt solution suspension is made, and this solution is used to dilute the blood serum, the dilution varying according as the test is desired to be more or less delicate. It makes no difference whether the micrococci are alive or dead, the agglutination reaction taking place as well with one as the other.

Curry's Method. Curry's method of performing the test[1] differs somewhat from that of Wright, and is thus described by him: "I used common glass tubing about 3 to 4 mm. in diameter, and made the observations macroscopically, and as a control made microscopic observations of drops of the fluid withdrawn by means of a platinum loop from the top, middle, and bottom of the tube. Tubes 7.5 cm. long and 3 to 4 mm. in diameter were made from glass tubing, and the bottoms were drawn out to a long, sharp point. These were sterilized and plugged with cotton in the dry sterilizer. Salt solution suspensions were made according to the method used by Wright. Bacteria were killed by heat at 60° C. for fifteen minutes, and 0.5 per cent. carbolic acid added. As a routine method one drop of blood serum was mixed with nineteen drops of normal salt solution, then equal parts of this mixed with the salt suspension of the culture of the micrococcus melitensis and placed in the small tubes of the sterile pipette. This equals

[1] "Malta Fever," Journal of Medical Research, vol. vi., No. 1.

a dilution of 1 to 40. A reaction was called positive and complete only when, in addition to the precipitation of the bacteria in the bottom of the tube, the supernatant fluid became clear.

Author's Method. In performing the serum test for Malta fever I have used practically the same method as that used for making the Widal test. A pure culture of the micrococcus, either upon agar or in bouillon, was used. The test may be performed either with the fresh serum or with a dry drop of blood, the latter being used preferably, as it is simpler and easier to procure. A drop of blood is secured upon a glass slide and diluted with enough sterilized water to dissolve it. A graduated pipette of very small calibre is used to make the dilution with the micrococcus. Having dissolved the drop of blood, a known portion is taken from it by the pipette and placed upon a clean slide; this is then diluted with a measured quantity of the bouillon culture or with a suspension of the agar culture made with sterilized water. The pipette is so graduated that a dilution can be made from 1 : 10 to 1 : 150. A cover-glass is then placed over the mixture, and this examined microscopically. In using the agar suspension the drop should first be examined so as to be sure there is no agglutination present before the blood is added. Preferably I have used a dilution of 1 : 75, although the agglutination reaction has been obtained with dilutions as high as 1 : 250 immediately. This method is easy of performance, all that is needed being the culture, the special graduated pipette, the cover-glass and slides, and the drop of blood. The method was used in all the cases described, and controls with a serum of other diseases—such as typhoid, dysentery, etc.—made at the same time, and it was found perfectly reliable.

Literature. The literature concerning the appearance of Malta fever among the soldiers of the United States army is very limited. The first case described was that of Dr. Musser, of Philadelphia, in the *Philadelphia Medical Journal* December, 1898. His case was that of an officer who contracted the disease in Porto Rico, and he was the first to draw attention to the fact that the disease was probably endemic in that island.

In the *Report of the Surgeon-General of the Army for 1899*, Walter Cox described a case occurring in Porto Rico and observed by him. The patient was a private of the Hospital Corps, aged thirty years. He came under observation January 14, 1899. He contracted fever in the guard-house of an old Spanish barracks, the fever commencing January 11, 1899. He complained of pain all over the body, especially in the bones and joints. Had two chills on successive days, but none afterward. This was at the commencement of the illness. The appetite was poor, and the bowels were at first loose and later constipated. The temperature curve showed daily remissions and reached normal

gradually. The morning temperature for a considerable time reached the normal point, but was 1, 2, or 3 degrees above normal toward evening. He was discharged from the hospital on April 3d, after about a week of normal temperature, but was readmitted April 7th, suffering again from fever. This attack was similar to the first. The blood was examined repeatedly for the malarial parasites as well as for the Widal reaction. A test with a culture of the micrococcus melitensis showed a marked agglutination in dilutions as high as 1 : 60.

Chamberlain, while on duty on the hospital ship "Relief," at Manila, P. I., observed two cases of the disease in soldiers, which were reported to the Surgeon-General of the Army. The men were in adjacent beds, and both presented mild attacks. The temperature curve was irregular, being neither markedly remittent nor undulating. The cases were first diagnosed as malarial fever, but the Malta fever reaction was performed at the laboratory of the First Reserve Hospital, and both were found positive. Examination of the blood for malarial parasites and the use of the Widal test both resulted negatively.

Curry and Strong, in 1900, reported cases occurring at the First Reserve Hospital. Strong performed an autopsy upon a man who had died from a continued fever of long duration. The post-mortem showed that it was neither typhoid nor malaria, and cultures from the case made by Curry resulted in the finding of the micrococcus melitensis. Inoculations into monkeys produced the typical symptoms of Malta fever. While performing these experiments Strong became infected and suffered from a typical attack of the fever. In another case the condition was discovered post-mortem, and cultures were obtained of the micro-organism. At this time two cases were observed in the wards of the hospital which gave the reaction with the micrococcus, and were undoubtedly cases of Malta fever.

The most valuable report of Malta fever occurring in soldiers of the army is that written by Curry and published in the *Journal of Medical Research*, vol. vi., No. 1. In this report Curry describes the cases which have come under his observation both in Manila and in the Army and Navy General Hospital, at Hot Springs, Ark. Besides the four cases of Malta fever observed in Manila, he observed in all eight cases of Malta fever in the hospital at Hot Springs. Four of these are described *in extenso*, the notes of the other four cases occurring in a note at the end of the report. All four of the latter cases were in a convalescent stage, the prominent symptoms being those of articular rheumatism, constipation, and frequent profuse sweatings. These cases were all diagnosed as articular rheumatism. Of the four cases described more fully all gave a marked serum reaction with the micrococcus melitensis when in a dilution as high as 1 to 300. None of the cases presented the symptoms found in the acute stage. The

symptoms complained of were pain in the articulations, constipation, and sweating, and all showed anæmia. These cases were all supposed to be suffering from chronic articular rheumatism.

In his recapitulation Curry says: "We have four cases of what was thought on admission to be chronic rheumatism. These cases have not improved under treatment nor by change to this favorable climate. Neither antirheumatic nor antimalarial treatment has benefited these men. In spite of treatment and favorable conditions, repeated and more or less regular recurrences of acute rheumatic pains and swellings and of fever have taken place. These conditions have lasted a long time—from six months, the shortest, to sixteen months, the longest of the series. The other prominent symptoms have been anæmia, profuse sweatings, and constipation. The blood examinations for malarial fever and for typhoid were negative, save in the case of one who had had severe typhoid fever two years ago. The clinical history of these cases corresponds with that of Malta fever, and the result of the serum test with the micrococcus makes it certain that the diagnosis of Malta fever in these cases is a correct one."

The important lesson to be learned from a study of the literature of Malta fever occurring in the United States army, and from the study of the cases described in this report, is that the condition is one not easily recognized clinically, and one apt to be mistaken for typhoid, malaria, or, in the chronic stage, for articular rheumatism. This being so, the great value of a microscopic examination of the blood and the performance of the serum test is at once proven. None of the cases observed by me was diagnosed as Malta fever, and in only one of them was there any suspicion of the occurrence of this disease. The two cases presenting the chronic symptoms would, in all probability, have been transferred to Hot Springs, Ark., for antirheumatic treatment, while in the two cases presenting the acute symptoms the patient would probably have been treated for either malaria or typhoid fever. In fact, in Case I., on account of finding malarial parasites at different times in the patient's blood, the treatment had been altogether that for malaria; and had a diagnosis of Malta fever been made more quickly much discomfort would probably have been saved the patient. The following conclusions may be drawn from the study of these cases:

1. There occurs in the tropics and subtropics a fever which may resemble in its acute stage either typhoid or malaria, and in its chronic stage articular rheumatism, caused by the micrococcus melitensis.

2. There are no pathognomonic symptoms of Malta fever. The symptoms observed are so inconstant and confusing that no one of them can be said to be typical of the disease.

3. A differential diagnosis of this fever is almost impossible in the majority of cases without the aid of the microscope and the serum test.

ON MULTIPLE SEROSITIS—THE ASSOCIATION OF CHRONIC OBLITERATIVE PERICARDITIS WITH ASCITES, WITH PARTICULAR REFERENCE TO THE "PERICARDITIC PSEUDOCIRRHOSIS OF THE LIVER" OF PICK AND THE "ICED LIVER" (ZUCKERGUSSLEBER) OF CURSCHMANN.[1]

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For purposes of study, cases of chronic adhesive or obliterative pericarditis may be divided into three classes: first, cases in which the pericarditis runs its course entirely devoid of symptoms and constitutes merely an accidental though interesting finding at the necropsy; second, cases in which, sooner or later, symptoms of disturbed or impeded cardiac action manifest themselves, and in which, from the physical signs, the obliterative pericarditis is more or less susceptible of diagnosis; and, third, cases characterized clinically by marked ascites, with little or no œdema of the legs, cases in which the diagnosis of cirrhosis of the liver is usually made and which at the necropsy reveal chronic obliterative pericarditis and certain morbid changes in other tissues and organs—notably pleuritis, peritonitis, perihepatitis, nutmeg liver, red atrophy of the liver, cirrhosis of the liver, etc. It is to the third class of cases that I wish to direct attention.

In the majority of cases when chronic adhesive or obliterative pericarditis gives rise to symptoms, the symptoms that arise are those of failing cardiac compensation—palpitation of the heart, dyspnœa, cough, cyanosis, generalized œdema, effusions into the several serous cavities of the body, etc. On the contrary, in the cases that simulate cirrhosis of the liver, clinically, the first symptoms are sensations of fulness, oppression, and weight in the upper abdomen, or there may be apparently a sudden onset with acute pain; the abdomen increases in size and may attain very large dimensions—due evidently to ascites that may necessitate repeated tappings (Rumpf's patient was tapped 301 times).

With increase in the amount of the ascites the abdominal walls become tense and painful, and the other subjective symptoms become

[1] Read, by invitation, at a meeting of the Johns Hopkins Hospital Medical Society, Baltimore, and at a meeting of the College of Physicians of Philadelphia.

markedly aggravated. There may be slight and transitory jaundice. Later œdema of the legs may develop. In a few cases œdema of the legs comes on early; it may remain but a short time, disappear, and not recur until shortly before the death of the patient. In rare cases it persists; but in the class of cases to which I refer it is always inconspicuous when contrasted with the excessive and constantly recurring ascites, and it scarcely attracts attention.

This symptom complex of obliterative pericarditis is of uncommon occurrence. While by no means unknown to the older writers, it attracted but little attention, and it was not until the communication of Pick, in 1896, that it became the subject of much discussion. Even at the present time it is overlooked by a number of systematic writers on diseases of the heart and of the liver, and a search through a number of recent text-books on medicine reveals little or no mention of it.

In the present state of our knowledge, it is to some extent a matter of personal opinion what cases should be included in the group of cases under discussion. From the point of view that I hope to elaborate, the earliest recorded case that I should include within this group was reported by van Deen in 1846. Subsequently cases were reported by Frerichs, Feierabend, Hambursin, Weiss, Vierordt, Tissier, Hirschler, Weinberg, Mott, Variot, Riedel, Henoch, Harris, Broadbent, and Dickinson. In 1884 Curschmann described his now well-known "zuckergussleber," or chronic hyperplastic perihepatitis—a disease characterized by a slow, insidious, and intermittent course, and persistent ascites, but without connective tissue hyperplasia in the liver. Although usually described as the "zuckergussleber" of Curschmann, this chronic hyperplastic perihepatitis was well known to a number of the earlier writers, being described by Hilton Fagge, in 1875, by Wilks and Moxon, in 1875, by Murchison, in 1868, by Bamberger in 1864, and by Rokitansky, in 1842. In 1895 a paper on the same subject, with the report of a case, was published by Rumpf. In 1896 Pick, reporting three cases, directed attention to the symptom complex simulating that of cirrhosis of the liver, but found at the necropsy to be due to obliterative pericarditis and associated changes in other tissues.

Pick pointed out that the recurring ascites with almost entire absence of œdema of the legs, the enlarged, firm, and somewhat irregular liver, and absent or slight jaundice, strongly suggested cirrhosis of the liver, and that the obliterative pericarditis usually escaped clinical recognition—although he was enabled to make the correct diagnosis during life in the third of his reported cases. Pick suggested for these cases the designation "pericarditic pseudocirrhosis of the liver"—a designation that has since found favor with some medical writers, and he

endeavored to establish an etiological relationship between the obliterative pericarditis, the enlarged liver, and the ascites. He stated that as a consequence of the pericarditis, which he looked upon as the primary disease, disturbances of circulation, with consecutive connective tissue hyperplasia in the liver, occurred, and that as a result of these ascites developed. In this class of cases he included the cases of "zuckergussleber" previously reported by Curschmann and by Rumpf, Following Pick's paper, the subject attracted considerable attention, reports of a number of cases appeared, discussions relating to the nature and the sequence of the morbid processes arose, and the interpretations of the lesions were many. Mention may be made of the papers by Heidemann, Hübler, Siegert, Werbatus, Nachod, Taylor, Ewart, Diemer, Schmaltz and Weber, Rose, Eisenmenger, Pick, Giradeau, Rosenbach, Hutinel, Türk, and others.

A disease that is identical with that under discussion has been well recognized in Italy, being known in some quarters as Concato's disease, polyorrhomenitis, or polyserositis. In 1891 Picchini published an extended report of the disease—basing his remarks upon personal observations and a critical study of the cases reported in the literature. Interesting papers were published by Cantu in 1894, and by Villani in 1895.

In 1898 Hager, a German author, writing on the subject, reviewed critically the Italian literature. Since the publication of Pick's paper, papers by Schupfer, Bozzolo, Galvagni, Patella, Caporali, and others have appeared. In France the disease is sometimes known as perivisceritis.

The only reports of cases by American writers that I have been able to find are those by Osler, in 1896, by Cabot, in 1898, and by Herrick, in 1902.

The subject has not been entirely neglected by systematic writers. Thus, in 1887, Rosenbach stated that pericardial obliteration is sometimes associated with extensive fibrous perihepatitis, enlargement of the liver, and ascites, "so that one might presume that enlargement of the liver, ascites, and pericardial synechiæ stand in causal relationship the one to the other." He refers to the subject also in his book on diseases of the heart. In 1890 Strümpell wrote that in cases of pericardial obliteration, he, as well as others, had sometimes observed marked ascites (at times associated with hydrothorax) without coincident œdema of the legs. In the latest edition of his text-book on medicine, referring to the subject, he states that all the cases presenting the symptom complex under discussion are not of one nature. In 1891 Leube wrote that pericardial obliteration sometimes gives rise to swelling of the liver and consequent ascites. In 1894 Schrötter wrote that pericardial obliteration sometimes gives rise to ascites before the occurrence of

general anasarca. The subject was referred to also by Osler, in the second edition of his text-book on *Practice of Medicine*, in 1895, by Quincke and Hoppe-Seyler, in 1899, and by Roberts, in 1900.

The subject may be illustrated by the report of the subjoined case. For the clinical notes, I am very much indebted to Dr. James C. Wilson, physician-in-chief, and to Dr. John B. Deaver, surgeon-in-chief, to the German Hospital.

Henry S., single, white male, aged thirty-one years, a native of Sweden, and a clerk by occupation, was admitted to the medical wards of the German Hospital, May 31, 1898, and the following history elicited:

He is the only child of his parents, both of whom are living and well. He has no knowledge of his having had any of the diseases of childhood. From an early age, however, he had been subject to convulsive seizures attended with unconsciousness. It is reported that his mother was similarly affected. The spells, as they occurred in the patient, came on at irregular intervals and lasted for from several minutes to about an hour. When about sixteen years of age they increased very much in frequency. At times he had a premonition of their oncoming. During some of the lighter attacks he did not lose consciousness entirely, that is, he was more or less aware of what was transpiring about him, but he was unable to speak. When about eight years of age he had severe pains in both groins and in the upper part of both thighs. At times these were so severe as to prevent his lying down.

At about the same time he experienced paræsthetic phenomena in the rectum—he felt as though there was something creeping about in the rectum. At the age of eighteen years he acquired gonorrhœa. One year later he had a severe attack of rheumatism that lasted about three months. Since then he has had a number of minor attacks of rheumatism, but none was severe enough to disable him. In 1890 he was treated in Bellevue Hospital, New York, for what he states was malaria. (A note from the Medical Superintendent of Bellevue Hospital, under date of March 12, 1901, states that the patient was treated in the hospital for malaria, from July 13 to 18, 1890. No details of his condition at that time are available.) For a short time during 1892 the patient was confined to an asylum. He had suffered a sunstroke and had become, he states, maniacal at times. Since then he has been troubled with disordered digestion, or "stomach trouble," as he expresses it. Although he is said to have been jaundiced at times, the most obtrusive symptom has been periodic pains in the right half of the abdomen just above the right iliac fossa. These occurred at first at intervals of about a month, later at intervals of two months or more.

During April, 1898, the patient was in the Jefferson Medical College Hospital for about two weeks. (Through the courtesy of Dr. H. A. Hare, I have ascertained that while in the hospital the patient was slightly jaundiced, and at times delirious, that he had several convulsions, and that although he complained of severe pain in the right upper abdominal quadrant and of tenderness over the region of the

gall-bladder, careful examination under ether failed to reveal any tumor in the region of the gall-bladder or other evidences of gallstones. The liver was slightly enlarged, and the superficial veins, especially those on the right side of the abdomen and the inner side of the right thigh were distended. The urine at this time was acid in reaction, had a specific gravity of 1025, contained 3.2 per cent. of urea, and neither sugar nor albumin. Examination of the blood revealed: erythrocytes, 5,200,000; leucocytes, 24,000; and hæmoglobin, 73 per cent. A differential count of the leucocytes revealed: small lymphocytes, 4 per cent.; large lymphocytes, 5 per cent.; transitional leucocytes, 4.9 per cent.; polynuclear leucocytes, 85.1 per cent.; and eosinophiles, 1 per cent.) Shortly after leaving the Jefferson Medical College Hospital the patient's abdomen began to enlarge, the pains in the right side of the abdomen became more severe and more frequent, so that he was incapacitated for work. He was admitted to the German Hospital complaining of severe pain and tenderness in the right upper abdominal quadrant, especially over the region of the gall-bladder, which was aggravated by deep inspiration; of pain over the pubes after micturition; at times of general pain in the right side of the abdomen; sharp cutting pains about three inches within the anus; attacks of vertigo; spots before the eyes; and of constipation of three years' duration. He smokes moderately, and formerly he consumed considerable quantities of alcohol.

On examination the only noteworthy sign was marked distention of the abdomen, due evidently to ascites. His liver dulness extended upward to the third rib. On June 2 the patient's abdomen was tapped, and 4400 c.c. of clear amber fluid was withdrawn. The fluid had a specific gravity of 1015, and contained a few erythrocytes and many leucocytes. The tapping relieved the patient very much, and afterward the liver dulness was found to be normal in area. There was marked tenderness over the region of the gall-bladder. Examination of the blood, on June 3, revealed the following: hæmoglobin, 82 per cent.; erythrocytes, 3,930,000, and leucocytes, 7300. A differential count of the leucocytes revealed the following: small lymphocytes, 11 per cent.; large lymphocytes, 9 per cent.; transitionals, 3 per cent.; polynuclear neutrophiles, 76.5 per cent., and eosinophiles, 0.5 per cent. On June 13 it was noted that the ascites was gradually reaccumulating, and the pains were becoming more frequent and more marked. On June 22 the patient was again tapped and 6700 c.c. of clear amber fluid was withdrawn. The fluid had a specific gravity of 1018, and contained a few erythrocytes and many leucocytes. On July 2 it was noted that the pain in the region of the gall-bladder had been absent since the second tapping. On this date the patient's feet were found to be slightly swollen—the first swelling of the feet since he had been in the hospital. (Upon inquiry he admitted that they had been slightly swollen on one previous occasion.) On July 9 the patient felt better than he had during the previous six months, and he was free from pain. On August 9, feeling well, he left the hospital of his own accord. His feet were not swollen at all, and he suffered no pain. His abdomen, however, contained considerable fluid, and was greater in circumference than it was when he entered the hospital. On the second day after his admission to the hospital his temperature was 102° F., and on several occasions subsequently it reached 100° F. Otherwise there was no

fever. His pulse was always low: on several occasions it was 80 per minute; usually it was between 60 and 68; and sometimes it was as low as 48 per minute. His urine was normal.

The patient was readmitted to the German Hospital, June 23, 1899, complaining of marked distention of the abdomen, pains in the region of the liver, at times of sharp shooting pain in the perineum, dyspnœa, slight pretibial œdema, diminution in the amount of urine voided daily, vertigo, and spots before his eyes. He stated that since he left the hospital his abdomen had been tapped twice. Inasmuch as the clinical diagnosis was cirrhosis of the liver, operation for the relief of the condition was proposed and acceded to by the patient. The operation was performed by Dr. John B. Deaver, July 3, 1899. In brief this consisted in irritating the peritoneum and stitching the omentum to the parietal peritoneum. The patient survived the operation four days, dying July 7, 1899.

The following are the notes of the necropsy performed by myself, July 8, 1899:

The body is that of a well-developed, fairly well-nourished male subject, with good bony development, good musculature, and moderate panniculus adiposus. There is post-mortem lividity in the dependent portions of the body; the skin is slightly jaundiced; there is no œdema of the extremities. In the median line of the abdomen there is a wound, about 16 cm. in length, apparently healing by first intention. The left pleural cavity is entirely obliterated by firm adhesions—the two layers of the pleura being dull, cloudy, whitish, and thickened. The left lung is about normal in size, and mottled grayish-black in color. Its air content is normal, its consistency firm, and it shows some hypostatic congestion in the dependent portions. Its section surface is smooth, moist, glistening, dark reddish in color, and exudes a quantity of frothy, blood-stained fluid. The lung crepitates throughout, and contains no tubercles. The bronchi are normal in size, they contain a small amount of mucus, and their mucous membrane is pale. The pulmonary vessels and the peribronchial lymph glands appear normal. The right pleural cavity is entirely obliterated by firm adhesions—the two layers of the pleura being dull, cloudy, whitish, and thickened. The right lung presents appearances similar to its fellow. The pericardium is firmly adherent to the anterior chest wall and the adjoining mediastinal tissues. The pericardial cavity is entirely obliterated, and such is the firmness of the adhesions that the two layers of the pericardium nowhere can be distinguished. In addition the pericardium is the seat of extensive calcareous infiltration, a large section of the heart being encased in a hard calcareous sheath. This calcareous sheath implicates the pericardium of the right ventricle, about one-half of the anterior and under surface of the right auricle, the left edge of the heart, the lowermost two-thirds of the left ventricle, the apex, and the diaphragmatic surface of the heart. This calcareous sheath appears to be made up of a single calcareous plate and not of a series of disunited plates. The pericardium of the left auricle, though firmly united with the adjacent parietal pericardium, is not the seat of calcareous infiltration. The several cavities of the heart appear to be normal in size, and they contain a moderate amount of dark, reddish-

brown, coagulated blood. The mitral orifice admits two fingers, the tricuspid orifice, three fingers. The mitral and tricuspid valve leaflets and the associated chordæ tendineæ are slightly thickened. The aortic and pulmonary valve leaflets are normal. Presumably all the valves are competent. The left ventricle (including the calcareous pericardium) measures 12 to 14 mm. in thickness, the right ventricle 5 to 8 mm., the left auricle 2 to 4 mm., and the right auricle 2 to 4 mm. The heart muscle is reddish-brown in color and firm in consistency. The coronary arteries and the aorta are normal. The heart and pericardium weigh 470 grammes. The omentum is normal in size and shape. The entire peritoneum is dull, lustreless, somewhat thickened, and intensely hemorrhagic. The coils of intestine are united to one another and to the other intra-abdominal organs by moderately firm, though friable, fibrinous adhesions. In some places an exudate may be stripped off in thin layers. The peritoneum contains also about 50 c.c. of serosanguinolent fluid (drainage had been provided at the time of the operation). The liver is firmly united to the under surface of the diaphragm by means of dense and firm adhesions, especially for a distance of about 6 cm. on both sides of the suspensory ligament. The capsule of the liver is thickened throughout, but especially on its upper surface, where in some places it is 4 mm. thick. In addition, on the capsule of the liver there is some fresh fibrinous exudate that may be stripped off; this is present especially on the under surface of the liver and for a short distance on the upper surface. The liver measures 22 cm. in length, 14 cm. in breadth, and 9 cm. in thickness. It weighs 1460 grammes. Its shape is normal, its consistency somewhat increased, its elasticity somewhat diminished, its surface somewhat irregular, and its edges rounded and hard. Its section surface is dull, moist, slightly granular, opaque, and light reddish-brown in color. The liver lobules are distinct, and there appears to be a slight increase in the connective tissue of the organ. The gall-bladder is normal in size and contains fluid bile. Its mucous membrane and wall are normal. The cystic, hepatic, and common bile-ducts are patulous. The spleen measures 10 cm. in length, 8 cm. in width, and 5 cm. in thickness. It is normal in shape and weighs 210 grammes. It is firm in consistency, and its capsule is slightly thickened and covered also with some fresh fibrinous exudate. The pulp is normal, the follicles rather distinct, and the trabeculæ slightly increased. The right kidney measures 11 cm. in length, 6 cm. in width, and 3 cm. in thickness. It is normal in shape and weighs 160 grammes. Its capsule strips readily, its surface is smooth, its color dark reddish-brown, and its consistency somewhat increased. The cortex is 7 mm. thick, and dark reddish-brown in color; the pyramids are congested. The calyces, pelvis, and ureter are normal. The left kidney weighs 170 grammes, and presents appearances similar to its fellow. The adrenals are normal. The bladder contains a small quantity of clear urine; its mucous membrane and wall are normal. The stomach is normal in size and position. It contains some turbid brownish fluid. The mucous membrane is congested and somewhat swollen. The duodenum and the remainder of the intestine are normal. The brain and spinal cord were not examined.

The anatomical diagnosis was as follows: acute hemorrhagic peritonitis; chronic adhesive pericarditis, with extensive calcification; chronic bilateral adhesive pleuritis; chronic perihepatitis (pericarditic

pseudocirrhosis of the liver of Pick); slight congestion of the liver, spleen, and kidneys.

Microscopic examination of the thickened pericardium revealed marked overgrowth of fibrous connective tissue with relatively few cells, and some extension of the newly-formed connective tissue into the interstices of the heart muscle. Careful examinations of sections from several regions revealed no evidences of tuberculosis. Examination of the thickened pleuræ revealed only fibroid thickening; no evidences of tuberculosis. Examination of the liver revealed chronic fibroid thickening of the capsule and some slight extension of connective tissue trabeculæ a short distance into the substance of the liver. In addition, evidences of acute inflammation were apparent, the round-cell infiltration being rather abundant. No evidence of tuberculosis could be detected. The liver itself revealed moderate distention of the central veins of the lobules and of the adjoining capillaries, with a moderate atrophy of the intervening liver cells. The cells of the periphery of the lobules showed slight fatty infiltration. The interlobular connective tissue possibly was slightly in excess of the normal, and contained a slight amount of round-cell infiltration. The spleen revealed the usual evidences of slight congestion and slight thickening of the trabeculæ.

The occurrence of marked ascites, with little or no œdema of the extremities in cases of failing cardiac compensation, though not very common, is by no means unknown. It was mentioned by Liebermeister in 1864, by Oppolzer in 1866, and it is observed by most clinicians of experience at the present time. The difficulties attending the diagnosis in these cases, however, are sometimes very great. The question whether an enlarged liver (in advanced cases a small liver) with ascites is to be referred to a primary or a secondary liver disease, if it presents itself to the mind of the clinician at all, may be difficult of solution. Light is shed on the case by the detecting of trustworthy evidence of cardiac valvular disease—in which case, especially if the patient be an adult, one has to determine whether the liver condition and the ascites are due to the heart disease or to an associated alcoholic cirrhosis of the liver. The diagnosis is even more difficult in cases of obliterative pericarditis, which appears to give rise to disproportionate ascites more frequently than does valvular disease of the heart. In these cases the pericarditis being usually latent and more or less insusceptible of diagnosis, the ascites is generally referred to a cirrhosis of the liver, rarely to tuberculous peritonitis, etc.

The cause of disproportionate ascites in cases of obliterative pericarditis has occasioned much discussion. Thus Weiss attributed it to changes in the bloodvessels of the peritoneum, the result of chronic peritonitis. He believed that in consequence of the pericardial obliteration general venous congestion occurs; that in consequence of the inflammation of the peritoneum, the peritoneum becomes a punctum minimæ resistentiæ; that transudation of serum occurs more readily from the altered vessels of the peritoneum than from other vessels of the body;

and that in consequence of the development of the ascites venous congestion in other parts of the body is relieved, and the development of œdema more or less prevented.

Mott believed that owing to the adherent pericardium interfering with the coronary circulation, the heart, instead of undergoing compensatory hypertrophy, as it sometimes does in the condition under discussion, slowly undergoes degeneration, and that this is doubtless hastened by the immense loss of fluid. He stated that, moreover, the thick adherent pericardium would interfere considerably with the elasticity of the walls of the heart and greatly modify its action as a suction pump during diastole, and that the circulation that this would affect most would be the portal, because here the blood has to pass through two sets of capillaries and against gravity. This is a view that is scarcely tenable, since, were it true, we should expect predominating ascites in all cases of failing cardiac compensation.

Weinberg attributed the ascites, with little or no œdema of the legs, to angulation of the inferior vena cava or the hepatic vein due to a right-sided pleural effusion. He assumed that in consequence of the angulation of the veins congestion and other changes in the liver, with consecutive ascites, occurred ; and he endeavored to support his opinions by citing the results of some experiments of Rosenbach's that appeared to show that such right-sided pleural effusion may cause angulation of the vena cava and congestion of the portal area. However, as pointed out by Pick, it is difficult to conceive of isolated compression of the hepatic vein, and compression or angulation of the inferior vena cava results in œdema of the legs rather than in ascites. Furthermore, in many of the cases there is no right-sided pleural effusion.

Rosenbach, while scarcely venturing to express a positive opinion on the subject, states that the ascites cannot be the result of simple insufficiency of the heart muscle, and he attributes considerable importance to the fibrous alterations in the liver capsule. He says, further, that the ascites must be the result of the operation of special conditions which, though associated with the heart affection, are not the direct result of diminution of the power of the heart; and that probably we have to do with an extension of the inflammatory process from the pericardium along the large veins to the serous covering of the liver, or vice versa, with the final development of connective tissue hyperplasia.

Pick, criticising adversely the opinions of Weiss, Mott, and Weinberg, points out that each of these writers in attempting to explain the occurrence of the ascites entirely overlooked that organ which, from the clinical course of the disease, one would be inclined to think most at fault—the liver. He states that in these cases the liver is described as rounded, increased in consistency, hemorrhagic, enlarged, markedly

irregular, granular, very firm, cirrhotic—in short, the appearances of the different stages of cyanotic induration, atrophic nutmeg liver, or the cardiac cirrhosis of the French. And inasmuch as other writers have observed prevailing ascites rather than œdema of the extremities in certain forms of heart disease, with similar secondary changes in the liver, he prefers to attribute the ascites in these cases of obliterative pericarditis to the alterations in the liver rather than to assume certain hypotheses. He says, further, that the question why in these cases ascites rather than generalized œdema occurs is intimately bound up with the question why in certain cases of congestion of the liver, in failing compensation of the heart in valvular disease, connective tissue proliferation occurs, whereas in other cases it does not occur; and that concerning this we know little definitely. For the time being he was content to point out the diagnostic features of the symptom complex in question. He believes that the associated peritoneal alterations are more or less accidental—that the thickening of the peritoneum results from the long-continued congestion and the persistence of the ascites, and that the thickening and the adhesions are in part due also to infection the result of repeated tappings.

Harris states: "There are two lesions, either of which may possibly occur as complications to the mediastinal and pericardial affection, and which could explain the ascites in such cases. In the first place, it is conceivable that chronic venous congestion of the liver produced by the cardiac dilatation may in some cases set up a chronic inflammation of the liver, a secondary periportal cirrhosis, which like the ordinary alcoholic cirrhosis would obstruct the portal circulation and produce ascites. We have seen that an increase of fibrous tissue in the liver is found in some of the cases of mediastino-pericarditis; but such a change does not appear to be the rule, and in the cases where it has been found it is questionable whether it has been sufficiently pronounced to produce portal obstruction and ascites therefrom. Furthermore, in one of my cases (Case II.) where the abdominal dropsy was such a prominent feature of the illness, the ascites was certainly not due to a cirrhotic liver, no marked periportal cirrhosis being found on microscopic examination. The second explanation of the occurrence of the ascites in the cases under consideration is that a chronic peritonitis ensues, and to it the ascites is due. Such chronic peritonitis in some instances may possibly be an independent affection, and one not directly connected with the mediastinal or pericardial lesion; in other cases it is conceivable that the chronic venous congestion due to the intrathoracic affection sets up the chronic peritonitis. Such a chronic peritoneal change was found in my second case, and was clearly sufficient to account for the ascites. That it is the explanation of the ascites in all such cases, of course, we do not say. It is quite possible that other

complications may, in some cases, occur which account for the development of ascites as a prominent feature of the case." After further discussion of the question, he says: "I am inclined, therefore, to think that the ascites which sometimes occurs in cases of mediastino-pericarditis, and which is unaccompanied by extreme anasarca of the lower extremities, is due, in some instances, at all events, to the onset of a peculiar form of chronic peritonitis. This chronic peritonitis may be possibly due to venous engorgement of the peritoneum consequent upon the dilatation of the heart or venous obstruction in the mediastinum, or it may occur so early in the case as to be probably independent of such venous stasis. In my second case the ascites was a prominent symptom from a very early period of the illness, and probably was independent of venous engorgement, which only appeared as a marked feature some time after the development of the ascites."

Heidemann, supporting the opinion of Weiss, states that in these cases we have to deal with a chronic inflammation of divers serous membranes; that the congestion, the result of the degeneration of the muscle of the heart, leads to ascites because the vessels of the peritoneum, on account of the chronic inflammation, constitute a locus minoris resistentiæ; that the associated cirrhotic processes in the liver observed in these cases result from an extension of the inflammatory irritant from the liver capsule and from the chronic congestion of the organ; and that in consequence of proliferation and shrinkage of the connective tissue on and in the liver the congestion and exudation into the peritoneal cavity are increased.

Eisenmenger, a pupil of Paltauf, states that it is quite true that in consequence of obliterative pericarditis marked ascites, with little or no œdema of the legs, occurs comparatively frequently, and that if the pericarditis is latent, the symptom complex bears a certain resemblance to cirrhosis of the liver. He states further that this symptom complex is not due, as is asserted by Pick, to connective tissue proliferation the result of disturbances of circulation in the liver, but that in different cases it is due to different causes. He emphasizes the etiological importance of distortions, compression, and angulations of the inferior vena cava, produced by a concomitant exudate or pleuropericardial thickenings; concomitant peritonitis in the transverse fissure of the liver; and, because the symptom complex is observed especially in young persons, the condition of the capillaries and small vessels in healthy young persons, in consequence of which œdematous transudations occur readily. Inasmuch, then, as the disease is not an anatomical entity, he disapproves of the designation "pericarditic pseudocirrhosis of the liver," suggested by Pick.

Without detailing the opinions of other writers, it suffices to state that the opinions of Mott and Weinberg are scarcely worthy of serious

consideration. In addition to the opinion of Eisenmenger, which is not supported by the report of any illustrative cases, there remain three opinions held by as many different groups of writers: the first, represented by Pick, Bozzolo, Nachod, Galvagni, Cabot, and others, attributes the ascites to changes in the liver the result of long-standing congestion; the second, represented by Weiss, Heidemann, Schupfer, Werbatus, and others, attributes the ascites primarily to the chronic peritonitis; and the third, represented by Harris, Osler, Patella, Siegert, and others, attributes the ascites to the combined action of both of these factors.

In view of these differences of opinion, it may not be unprofitable, from a study of the cases reported in the literature, to ascertain the more likely cause of the predominating ascites, and in general the nature of the disease in question. From the subjoined table I have omitted all cases in which the ascites was merely a part of generalized dropsy and effusions into the several serous cavities of the body; cases, of which Wagner's and Türk's serve as examples, in which the lesions were a disseminated tuberculosis of the organs, as well as of the serous membranes; and, for instance, a second case reported by Diemer, in which obliterative pericarditis and atrophic cirrhosis of the liver occurred, but in which there was no note of ascites. I have been obliged reluctantly to omit also a number of cases reported by Italians —Galvagni, Bozzolo, Patella, and Caporali. Their reports were unavailable in the original, and the abstracts at my disposal were not sufficiently complete to enable me to incorporate them in the table.

Reporter.	Sex and age.	Duration, years.	Ascites.	Œdema.	Pericardium.	Right pleura.	Left pleura.	Peritoneum.	Liver.	Spleen.	Remarks.
Van Deen, 1846	M. 40	2	Constant.	Subsequent to ascites.	Markedly thickened and firmly adherent to the heart.	Adherent throughout	Adherent throughout	Thickened throughout; many adhesions.	Chronic perihepatitis; liver otherwise normal.	Chronic perisplenitis; spleen otherwise normal.	The peritoneum of the under surface of the diaphragm and of the upper portion of the abdomen was least affected; pericarditis believed to be the primary affection, the pleuræ and the peritoneum being affected secondarily, the peritoneum through spreading of the inflammation through the diaphragm.
Frerichs, 1861	F. 38	2	Constant.	Constant, but moderate.	Firmly adherent throughout.	Adherent throughout	Adherent throughout	Cloudy, injected, and much thickened in many places.	Marked chronic perihepatitis; cirrhosis; liver one-third smaller than normal.	Marked chronic perisplenitis; spleen enlarged.	It is believed that the liver induration was caused by a peritonitis, the symptoms of which preceded by two years symptoms referable to the liver.
Feierabend, 1866	M. 50	4	Constant.	No.	Adher'nt and markedly calcified, especially the anterior surface; the apex free.	.....	.....	.....	Marked cirrhosis.	Enlarged.	Pericarditis 23 years previously; four tappings for relief of the ascites; the clinical diagnosis was cirrhosis of the liver with secondary gastro-intestinal catarrh.
Hambursin, 1869	M. 50	4	Constant.	Only shortly before death.	Chronic adhesions to the right of the base of the heart and to diaphragm; also fluid.	Chronic adhesions.	Normal.	Chronic adhesions and thickening.	Marked chronic perihepatitis; liver small, nutmeg, and cirrhotic.	Normal.	The disease is presumed to have begun in the liver capsule and to have implicated the pericardium subsequently.
Weiss, 1876	F. 51	1½	Constant.	Constant; moderate.	Thickened and adherent throughout.	Obliterated	Obliterated	Thickened & opaque; many adhesions.	Chronic perihepatitis; liver large and firm.	Chronic perisplenitis.	Presumed to have followed rheumatism; the anatomical diagnosis was total concretion of the abdominal and thoracic organs.
Weiss, 1876	F. 14	2	Constant	Only shortly before death.	Obliterated.	Fluid.	Obliterated	Thickened & opaque; many adhesions.	Chronic perihepatitis; liver firm.	Chronic perisplenitis.	Followed typhoid fever; many tappings for relief of the ascites.
Vierordt, 1884	F. 20	6	Constant.	Slight late in the course of the disease.	Obliterated.	Chronic adhesions.	Normal.	Thickened & opaque; many adhesions	Chronic perihepatitis; cirrhosis.	Chronic perisplenitis; spleen enlarged.	Presumed to have begun in the liver capsule; standstill for 1 year; 34 tappings (460 litres of fluid) for relief of the ascites.

Vierordt, 1884	F. 35	6	Constant.	Slight and transient.	Obliterated; marked calcification.	Obliterat'd; thickened.	Obliterat'd; thickened.	Thickened & opaque; many adhesions.	Marked chronic perihepatitis (zuckergussleber); liver nutmeg.	Marked chronic perisplenitis (zuckergussmilz); spleen enlarged.	Presumed to have started in the pericardium; standstill for several years; several tappings for relief of the ascites; it is suggested that the peritonitis and the chronic inflammatory changes in the pericardium stand in some relationship to each other.
Curschmann, 1884	F. 54	6½	Constant.	No.	Obliterated; thickened.	Obliterat'd; thickened.	Acute serofibrinous inflammation.	Thickening, induration, opacity, and adhesions of the peritoneum of the upper half of the abdomen.	Diffuse chronic hyperplastic perihepatitis; compression and reduction in size(⅓) of the otherwise unaltered liver.	Marked chronic perisplenitis; spleen double the normal size.	Many tappings for relief of the ascites; standstill for a year and a half; recent tuberculous peritonitis at the necropsy.
Tissier, 1885	F. 51	10	Constant.	Yes.	Obliterated; calcification at left edge anteriorly & posteriorly; apex free.	Fluid.	Fluid.	Thickening, opacity and adhesions.	Marked chronic perihepatitis (zuckergussleber); liver enenlarged and nutmeg.	Chronic perisplenitis.	Several punctures for relief of the ascites.
Hirschler, 1886	F. 48	...	Constant.	Slight.	Obliterated.	Fluid.					
Weinberg, 1887	M. 19	⅓	Constant, though preceded by symptoms of acute pleuritis.	Subsequent to the ascites.	Thickened and obliterated.	Fluid.	Fluid.	Chronic peritonitis.	Chronic perihepatitis; liver nutmeg.	Enlarged.	Two tappings for relief of the ascites; process tuberculous, the result of primary infection of the pericardium by a tuberculous bronchial lymph gland.
Weinberg, 1887	F. 18	⅔	Constant.	Late in the course of the disease.	Thickened and obliterated.	Obliterated	Obliterated	Thickening, opacity and adhesions.	Chronic perihepatitis (not so marked on diaphragmatic surface as elsewhere); liver congested; weight 2050 grammes.	Normal.	Fifteen tappings for relief of the ascites; process tuberculous, the result of primary infection of the pericardium by tuberculous bronchial lymph gland.
Mott, 1887	M. 17	2½	Constant.	Only shortly before death.	Thickened and obliterated.	Thickened and obliterated.	Thickened and obliterated.	Inflammatory lymph	Nutmeg; weight 54 ounces.	Normal.	Several tappings for relief of the ascites; process began as a pleuropericarditis.
Mott, 1887	M. 23	1½	Constant.	Subsequent to and less than the ascites.	Thickened and obliterated.	Recent serofibrinous exudate.	Thickened and obliterated.	.....	Enlarged; weight 5 pounds.	Congested; weight 18 oz.	Process began as a pleuropericarditis.

Reporter.	Sex and age.	Duration, years	Ascites.	Œdema.	Pericardium.	Right pleura.	Left pleura.	Peritoneum.	Liver.	Spleen.	Remarks.
Variot, 1888	M. 51	...	Constant.	.....	Obliterated; marked calcification of anterior surface of right ventricle, left auricle, right edge, and posterior surface.	Chronic adhesions and fluid.	Chronic adhesions.	Chronic adhesions.	Marked chronic perihepatitis (zuckergussleber); liver enlarged.	Somewhat enlarged.	Clinical diagnosis: mitral insufficiency and right-sided pleural effusion.
Riedel, 1892	M. 19	15	Constant.	Only shortly before death	Thickened and obliterated.	Chronic adhesions, thickening and fluid.	Chronic adhesions, thick'ning, and fluid.	Entire peritoneum markedly thickened and adherent.	Marked chronic perihepatitis (zuckergussleber) with extension of connective tissue into the liver substance.	Chronic perisplenitis: spleen enlarged.	Heart, lungs, liver, and spleen—zuckerguss; several tappings for relief of the ascites. Process presumed to have begun in the different serous membranes at the same time, although it is admitted that the disease may have begun in the pericardium as a complication of pertussis, and subsequently have implicated the other serous membranes by contiguity of structure. Standstill for eight years.
Cantu, 1894	F. 41	...	Constant.	.....	Thickened and obliterated.	Fluid.	Fluid.	.....	Nutmeg.	Congested.	
Rumpf, 1895	F. 49	16	Constant.	Of left leg.	Thickened and obliterated.	Chronic adhesions and fluid.	Chronic adhesions and thickening.	Thickening, opacity and adhesions.	Diffuse chronic hyperplastic perinephritis (zuckergussleber); compression of the otherwise unaltered liver.	Chronic perisplenitis; spleen moderately enlarged.	301 tappings for relief of the ascites; process presumed to have begun in the pericardium; acute pericarditis at the age of 33 years.
Henoch, 1895	M. 5	14 days (?)	Constant.	Constant.	Thickened and obliterated.	Thickened and adherent.	Thickened and adherent.	.....	Chronic perihepatitis; liver enlarged and cirrhotic.	Enlarged.	Presumed to be syphilitic.
Harris, 1895	M. 8	3½	Constant.	Slight.	Thickened and obliterated.	Thickened and obliterated.	Thickened and obliterated.	Thickening, opacity and adhesions.	Marked chronic perihepatitis; liver nutmeg; little or no cirrhosis.	Marked chronic perisplenitis; spleen congested.	Many tappings for relief of the ascites; old tuberculous focus in the apex of the right lung; tuberculous arthritis of the right elbow.
Broadbent, 1895	F. 16	½	Constant.	Present, but much less than the ascites.	Thickened and obliterated.	.....	.....	Recent miliary tuberculosis.	Enlarged and nutmeg.	.....	Tuberculous focus in the apex of the left lung; striking feature of the case "the constant accumulation of fluid in the peritoneal cavity."

Pick, 1896	M. 47	4	Constant.	Slight.	Thickened and obliterated.	Fluid.	Chronic adhesions.	General fibrous peritonitis.	Chronic perihepatitis; liver enlarged and nutmeg.	Chronic perisplenitis: spleen congested.	Many tappings for relief of the ascites.
Pick, 1896	M. 26	8	Constant.	Late in the course of the disease.	Thickened and obliterated; extensive calcification.	Fluid.	Fluid.	.....	Enlarged and cirrhotic.	Enlarged five times the normal size.	Many tappings for relief of the ascites.
Pick, 1896	M. 24	2	Constant.	Subsequent to the ascites.	Obliterated; extensive calcification.	Chronic adhesions.	Chronic adhesions.	Thickening, opacity and adhesions.	Perihepatitis and cirrhosis.	Perisplenitis.	Process tuberculous; correct diagnosis during life.
Osler, 1896	F. 14	3½	Constant.	General at first; disappeared; reappeared; but always slight.	Thickened and partly obliterated.	Chronic adhesions.	.....	Thickening, opacity and adhesions.	Marked chronic perihepatitis and cirrhosis.	Perisplenitis; spleen enlarged and congested.	Correct diagnosis during life; extreme cyanosis of the hands and feet, and subcutaneous nodules about the knuckles, wrists, and elbows; 121 tappings for relief of the ascites.
Dickinson, 1896	F. 17	5	Constant.	Much less than the ascites.	Thickened and obliterated.	Chronic adhesions.	Obliterated	.....	Enlarged (64 oz.) and nutmeg; capsule thickened.	.....	26 tappings for relief of the ascites.
Heidemann, 1897	F. 15	1	Constant.	Subsequent to the ascites.	Obliterated.	Chronic adhesions and fluid.	Serofibrinous exudate.	Fibrous peritonitis, especially of Douglas' cul-de sac.	Small nutmeg and cirrhotic.	Somewhat enlarged.	Pericarditis one year previously; 23 tappings for relief of the ascites.
Schupfer, 1897	M. 44	4¾	Constant.	Slight at beginning; disappear'd and recurred shortly before death.	Obliterated.	Thickened and obliterated.	Thickened and obliterated.	Chronic fibrous hyperplastic peritonitis.	Marked chronic perihepatitis with extension of the connective tissue into the liver substance.	Perisplenitis.	Presumed to have begun at the same time in the different serous membranes; standstill for one year.
Cabot, 1898	M. 18	6	Constant.	Slight at intervals.	Obliterated.	Chronic adhesions and fluid.	Chronic adhesions and fluid.	.....	Enlarged and nutmeg.	.....	Several tappings for relief of the ascites.
Siegert, 1898	M. 19	9	Constant.	General at the beginning; disappeared, and recurred for short periods, & again before death.	Thickened and obliterated.	Chronic adhesions.	Chronic adhesions.	Thickening, opacity and adhesions.	Chronic perihepatitis with extension of connective tissue into the liver substance; liver congested.	Perisplenitis; spleen slightly enlarged.	Presumed to have begun in the pericardium; standstill for two and a half years; more than 100 tappings for relief of ascites.
Werbatus, 1898	M. 42	6	Constant.	Subsequent to the ascites.	Thickened and obliterated.	Thickened and obliterated.	Thickened and obliterated.	Thickening, opacity and adhesions.	Chronic perihepatitis; atrophic nutmeg liver and cirrhosis.	Chronic perisplenitis and congestion.	

Reporter.	Sex and age.	Duration, years.	Ascites.	Œdema.	Pericardium.	Right pleura.	Left pleura.	Peritoneum.	Liver.	Spleen.	Remarks.
Nachod, 1898	M. 6	1	Constant.	Slight at beginning; disappear'd and reappeared shortly before death.	Thickened and obliterated.	Extensive adhesions.	Extensive adhesions.	Chronic adhesions.	Liver firmer than normal; many caseous nodules in the capsule.	Enlarged; capsule thickened and contained many caseous nodules.	Nine months prior to death, with the idea that the ascites was due to tuberculous peritonitis, cœliotomy was performed, but the peritoneum was found entirely normal; the pericarditis evidently was primary; some bronchial glands were tuberculous.
Taylor, 1898	F. 42	1½	Constant.	Subsequent to the ascites.	Thickened and obliterated.	Thickened and obliterated.	Thickened and obliterated.	Univers'lly thick and opaque.	Perihepatitis and compression of the liver.	Perisplenitis; spleen hard and small.	
Ewart, 1899	F. 49	4	Constant.	Slight.	Obliterated and calcified.	.....	.....	Adhesions and thickening.	Enlarged and congested.	Perisplenitis.	Operated upon for the cure of a supposed cirrhosis of the liver; previously to the operation fifty-two tappings for the relief of the ascites.
Diemer, 1899	M. 38	1½	Constant.	Present at first; disappeared, and reappeared.	Obliterated; extensive calcification, wide calcareous circlet about both ventricles; apex free.	Thickening and chronic adhesions.	Normal.	Diffuse thickening and adhesions.	Chronic fibrous perihepatitis (zuckergussleber); diffuse syphilitic cirrhosis.	Chronic perisplenitis (zuckergussmilz); chronic congestion.	Many tappings for relief of the ascites.
Schmaltz and Weber, 1899	F. 42	5	Constant.	Slight subsequent to the ascites.	Obliterated by recent adhesions.	Slight adhesions.	Adhesions.	Chronic adhesions.	Marked chronic perihepatitis (zuckergussleber); no connective tissue increase or marked congestion.	Marked chronic perisplenitis (zuckergussmilz); congestion.	Many tappings for relief of the ascites; standstill for two years.
Herrick, 1902	M. 20	4	Constant.	Present at first; disappeared and recurred.	Obliterated; extensive calcification of left half anteriorly & posteriorly, and of diaphragmatic surface.	Obliterated and thickened; small tuberculous sac.	Obliterated and thickened.	Smooth except for the perihepatitis and perisplenitis.	Chronic perihepatitis; liver firm; weight 2235 grammes; microscopic examination showed "cardiac cirrhosis."	Perisplenitis; spleen greatly enlarged.	Process tuberculous; several tappings for relief of the ascites and the pleural effusion; standstill for one year.
Kelly, 1902	M. 31	7	Constant.	Slight and transitory.	Obliterated; extensive calcification of both ventricles.	Thickened and obliterated.	Thickened and obliterated.	Recent hemorrhagic peritonitis	Chronic perihepatitis; congestion.	Congestion.	Several tappings for relief of the ascites.

Of the 39 cases in the table, 21 occurred in males, and 18 in females. The ages of the patients were as follows: 3 were under ten years of age; 13 were between eleven and twenty years; 3 were between twenty-one and thirty years; 5 were between thirty-one and forty years; 11 were between forty-one and fifty years; and 4 were between fifty-one and fifty-four years. This summary well illustrates a fact commented upon by a number of writers, namely, the prevalence of the disease among young subjects. Presumably, it indicates also that should the patient survive the twentieth year he or she is likely to live until the fourth decade of life. In 3 of the cases the duration of the disease was not ascertainable. In 26 cases the duration was two years or more; in 19 cases it was four years or more; in 1 case it was ten years; in 1 case it was fifteen years; and in 1 case it was sixteen years. In 1 case (Henoch's) the duration is put questionably at fourteen days. The striking clinical feature of all of the cases was the constant and predominating ascites, an ascites that necessitated many tappings and continuously recurred—whence the diagnosis in many cases of cirrhosis of the liver, in other cases of peritoneal tuberculosis. In most of the cases œdema of the legs was absent until shortly before death. In a few cases œdema was slight throughout the course of the disease, and in several of these it increased moderately or considerably shortly before death. In other cases it was present early in the course of the disease, but it soon disappeared, although the ascites persisted, and it did not recur until shortly before death; or it reappeared and disappeared irregularly throughout the course of the disease.

With regard to the anatomical lesions—in one case (Schmaltz and Weber's) the pericardium was obliterated by recent adhesions. In the remaining 38 cases the pericardium was thickened and obliterated by chronic adhesions—in almost all of the cases entirely obliterated, in one or two cases only partly obliterated. In 10 of the cases there was, in addition, more or less extensive calcification of the pericardium —the case herewith reported being the most marked example of this condition that I have encountered.

There is no statement with regard to the condition of the right pleura in 3 cases. In 1 case the right pleura contained recent serofibrinous exudate, in 6 cases it contained fluid, in 12 cases there were more or less extensive chronic adhesions, and in the remaining 17 cases the pleura was entirely obliterated and generally thickened. There is no statement with regard to the condition of the left pleura in 5 cases. In 3 cases the left pleura was normal, in 2 cases it contained recent serofibrinous exudate, in 4 cases it contained fluid, in 10 cases there were more or less extensive chronic adhesions, and in the remaining 15 cases the pleura was entirely obliterated and generally thickened. In most of the cases in which there were chronic adhesions fluid also was

present, and in most of the cases in which there were thickening and obliteration of the pleura and pericardial sacs there were also external adhesions binding the pericardium to the chest wall and external surface of the pleura and the adjacent tissues of the mediastinum. The summary well illustrates the more marked involvement of the right pleura as contrasted with the left pleura—a subject that has been much commented upon recently. There is no statement with regard to the condition of the general peritoneum in 8 cases. In 1 case there was recent hemorrhagic peritonitis, in 1 case recent miliary tuberculosis, and in 1 case inflammatory lymph, and in the remaining 28 cases there were more or less extensive chronic adhesions.

There is no statement with regard to the condition of the liver in 1 case. In 28 cases chronic perihepatitis was noted, and in 31 cases there was either chronic perihepatitis or chronic peritonitis or both. The liver itself was reported to be nutmeg in appearance in 14 cases, cirrhotic in 8 cases, large and firm in 5 cases, normal aside from compression in 4 cases, nutmeg and cirrhotic in 4 cases, and in 3 cases there appeared to be only extension of connective tissue from the thickened capsule into the substance of the organ. Perisplenitis was noted in 23 cases. There was no statement with regard to the condition of the spleen itself in 12 cases. In 23 cases it was congested, in 1 case it was small and hard, and in 3 cases it was normal.

From this tabulation and summary two facts stand out prominently: 1. That although all the cases presented ascites as the striking clinical feature and revealed obliterative pericarditis at the necropsy, yet that organ that we might presume to be most at fault—the liver—presented a variety of lesions in the different cases; and 2, that in all the cases more than one serous membrane, in some of the cases all the serous membranes were diseased. The feature possessed by the cases in common, therefore, is widespread disease of the serous membranes, and the most common lesion is chronic hyperplastic serositis.

In some cases there is a clear history of the repeated occurrence of inflammation of one or more serous membranes; in other cases the disease was latent and entirely unsuspected during life. In some cases the history points definitely to a certain serous membrane as the point of departure of the disease, to the membrane whence the inflammatory process spread to the other membranes. In this connection, however, we should bear in mind that the serous membrane disease that attracted attention in some of these cases began acutely, and that such disease of a serous membrane may just as well be the consequence as the cause of a latent inflammation of some other serous membrane. Thus it is that in some of the cases with multiple involvement of the serous membranes, different writers interpret the necropsy findings differently. Some attribute the symptom complex to a primary pericarditis with consecu-

tive pleuritis and peritonitis; others hold the opposite view, and look upon the peritonitis as the primary event, and attribute the pleuritis and pericarditis to extension of the inflammation through the diaphragm from a perihepatitis; others hold that the perihepatitis is the primary disease and that from this by continuity and contiguity of structure the peritonitis and the pericarditis arise; and, finally, still others hold that all of the serous membranes become infected with the same noxious agent at the same time.

From this point of view Picchini distinguishes four groups of cases of multiple serositis or polyserositis: 1. Cases in which by means of careful inquiry the point of origin of the disease, that is, the serous membrane first affected, as well as the order of the involvement of the other serous membranes, may be determined. 2. Cases in which on inquiry the point of origin of the disease may be determined, but in which the first examination of the patient reveals that several serous membranes are already affected, although they manifest no clinical symptoms. 3. Cases in which the history reveals that from the beginning several serous membranes have been affected. 4. Cases in which from the history it cannot be determined whether the disease began with inflammation of one or more serous membranes. Of the 50 cases observed by Picchini, 37 belonged to the first group; 11 to the second; 1 to the third, and 1 to the fourth group. Of 110 collected by Picchini (50 observed by himself and 60 collected from the literature) the peritoneum was involved in all, although this was recognized clinically in only 13 of the cases. This peritonitis was not only the most frequent, but also the most important lesion; it dominated the situation. Pleuritis was present in 109 cases, in 73 of which it was bilateral. The pericardium was least frequently involved—only in 9 of 50 cases. This fact is deemed evidence of great resistance on the part of the pericardium.

De Renzi states that in multiple serositis the peritoneum is usually involved first; then the right pleura, and then the pericardium. If, however, the right pleura should be involved first, the disease then extends to the peritoneum, thence to the left pleura and the pericardium. In some cases, however, this mode of progression of the disease is not preserved, as sometimes a pericarditis that usually is not to be diagnosticated develops first. De Renzi states further that the disease is characterized by the fact that it remains localized to the serous membranes; that it does not implicate the intra-abdominal and intrathoracic organs; that it pursues a remarkably slow and insidious course; that it gives rise to the exudation of large quantities of serofibrinous fluid; and that the fluid portion of the exudate tends to become absorbed, in consequence of which fibrous adhesions with complete obliteration of the serous cavities result.

Presuming, then, that the inflammation may begin in any serous membrane, it is evident that the clinical manifestations may vary, depending upon the serous membrane first affected. This is commented upon by a number of writers, and it is discussed at length by Siegert, who points out that although the chronic perihepatitis and the resultant ascites dominate the clinical picture, the clinical picture nevertheless assumes quite different aspects depending upon whether the disease begins in one or more serous membranes. Thus, if the liver capsule is first affected ascites occurs as an inflammatory exudate. If after the lapse of some time the perihepatitis leads to compression of the liver and the portal radicles, another factor contributing to congestion and ascites is added. Thus it is that ascites is the prominent symptom in those cases of multiple serositis in which the disease begins in the peritoneum. Later in the course of the disease the marked increase in the intra-abdominal pressure occasioned by the large amount of the ascites, as well as the spread of the inflammatory process to the pleura and the pericardium, may lead to congestion in the area of collection of the inferior vena cava, so that to the ascites œdema of the legs is added.

That multiple serositis may begin in one or the other pleura must be conceded, and that such is really the case is rendered likely by the history of early and apparently primary pleuritis in several of the cases tabulated. Especial interest, however, attaches to primary involvement of the pericardium. In the reports of some of the cases tabulated there appears a note that acute pericarditis occurred some years prior to the development of the symptoms that interest us at present, and in other of the cases the nature and the extent of pericardial lesions warrant the assumption that these were the primary lesions—for instance, the cases reported by Feierabend, Vierordt, Weinberg, Mott, Riedel (?), Rumpf, Pick, Osler, Heidemann, Siegert, Nachod, Ewart, and my own case. When the pericardium is primarily affected certain features in the clinical course of the disease may occur that possess especial interest and diagnostic importance. Whereas in those cases in which the peritonitis or perihepatitis is the primary event, ascites occurs early and is succeeded by œdema only late in the course of the disease, in the cases beginning with pericarditis œdema of the legs may occur early—the consequence of early and transitory insufficiency of the myocardium. In cases in which this occurs the œdema usually soon disappears and is succeeded by ascites, which assumes and maintains the ascendency—for instance, cases reported by Vierordt, Broadbent, Rumpf, Osler, Dickinson, Schupfer, Siegert, Nachod, and Diemer. However, as pointed out by Siegert, the absence of œdema of the legs in the presence of ascites early in the course of the disease is no evidence of primary implication of the peritoneum rather than of the pericardium, since

it is well known that chronic obliterative pericarditis frequently runs a course entirely devoid of symptoms.

The cause of this obliterative pericarditis, as well as the cause of the multiple serositis in general, has occasioned considerable discussion. Certain of the infective diseases, such as typhoid fever, pertussis, malaria, syphilis, and rheumatism, are given as etiological factors in a number of the cases tabulated. In a number of the cases the lesions are of extremely obscure or unknown etiology, whereas, in other cases the provoking agent was certainly the tubercle bacillus. The fact that possesses considerable interest in this connection is that during recent years medical writers have become more and more inclined to look upon many cases of chronic obliterative pericarditis (as well as disease of other serous membranes) as tuberculous in nature, and this even in the absence of clear evidence of tuberculosis. This has been insisted upon for a number of years by the German and the Italian writers, and it is emphasized by Riesman and by Wells in their recent communications. According to a number of writers the disease is always tuberculous in nature; other writers, however, are disposed to admit the occasional operation of other etiological factors, inasmuch as it has not been possible to demonstrate the tuberculous nature of all cases by either macroscopic, microscopic, or bacteriologic examinations. The important fact to bear in mind is that many cases apparently non-tuberculous are in reality due to the tubercle bacillus, and that in some cases characteristic tuberculous lesions may be detected by microscopic examination of the tissues, and that the tubercle bacillus may be recovered from some of the lesions by appropriate bacteriologic and inoculation procedures. Presumably, also, the patient would react to tuberculin injections. On the other hand, that a number of cases are not tuberculous must be conceded. In my own case careful microscopic examination of the tissues failed to disclose any tuberculous lesions. I would suggest that in my own case, as well as in other cases, antecedent rheumatism possesses considerable etiological importance. In some cases chronic nephritis may be the etiological factor; whereas in other cases the disease seems to develop from cholelithiasis with cholecystitis and pericholecystitis (localized peritonitis).

An important and interesting fact especially insisted upon by the Italian writers is that not every case of general tuberculosis that implicates the serous membranes and gives rise to chronic fibrous lesions belongs to the group of cases under discussion. Picchini states that the cases under discussion differ from the ordinary cases of serous membrane tuberculosis in that in their etiology heredity appears to play no rôle; that the disease does not appear to affect especially persons of phthisical or tuberculous habitus; that the inflammations of the serous membranes set in insidiously, much less acutely than do the

ordinary cases of tuberculous inflammation; that they may remain latent for a long time; and that the lesions remain localized to the serous investment of the organs and are unassociated with tuberculous lesions of the lungs, as is so common in the ordinary cases. A study of the cases reported in the literature bears out the reasonableness of this view.

A marked susceptibility of the serous membranes and a certain immunity of the organs to the cause of the disease—presumably the tubercle bacillus in many of the cases—appear to be striking features of the cases. Nevertheless, there seem to be border-line cases and cases representing varying degrees of infection with the tubercle bacillus: 1. Cases in which the lesions are confined strictly to the serous membranes. 2. Cases in which the lesions involve, especially the serous membranes, but in which one or several tuberculous foci may be found in the body—for instance, the cases reported by Weinberg, Harris, Broadbent, Pick, and Nachod. 3. Cases in which the serous membrane disease represents but a part of a general tuberculous infection (not considered in this communication). That this is probably true is borne out by the fact that in one or two of the cases the fatal termination was brought about by an acute disseminated miliary tuberculosis. Cantu accounts for the peculiarities of the disease as contrasted with the ordinary cases of tuberculosis of the serous membranes by assuming that it is due to a special form of the tubercle bacillus. On account of the length and arrangement of the tubercle bacilli in the newly formed connective tissue in his case, he assumed that the bacillus operative was allied to that form peculiar to birds.

Some discussion has been occasioned by certain writers—Pick, Schupfer, Werbatus, Heidemann, and others—including the group of cases under consideration, the cases of "zuckergussleber," reported by Curschmann, Rumpf, and Hübler. Reference to the table will show that the cases of Curschmann and of Rumpf are in reality cases of multiple serositis, that in them the lesions of the serous membranes were widespread. In Hübler's case, as well as in a number of cases reported by Hale White, the lesions were confined to the peritoneum. Inasmuch, however, as the lesions in these cases are similar to the more widespread lesions in the other cases, it is warrantable to group all of them in the same category as cases of more or less extensive serositis. The cases differ among themselves in the extent and intensity of the serous membrane involvement, but in all the cases the lesions are alike. We have to explain, however, the greater intensity of the lesions about the liver in the cases in which the peritoneum is the only serous membrane involved, as well as in other cases in which the pleuræ and the pericardium also are involved.

The intensity of the lesions about the liver finds its explanation in

certain facts known regarding the anatomy, physiology, and pathology of the peritoneum and its circulation. The facts that interest us at present have been worked out by a number of investigators, and they have been confirmed and summarized by Clark about as follows: Fluids and solids may pass through the endothelial layer of the peritoneum, the fluids in many places, the solid particles only through the central tendon in the diaphragm. Minute particles are carried in an incredibly short time from the peritoneal cavity through the diaphragm into the mediastinal lymph vessels and glands, and thence into the blood circulation, by which they are distributed to the abdominal organs, to appear in the collecting lymph glands of these organs. The leucocytes are largely the bearers of foreign bodies from the peritoneal cavity through the diaphragm into the mediastinal lymph vessels and thence into the blood circulation. There is normally a force in the peritoneal cavity which carries the fluids and foreign particles toward the diaphragm, regardless of the posture of the patient, though gravity can greatly favor or retard the current. It is pointed out also by Clark that under normal circumstances the peritoneum can dispose of pyogenic organisms in varying number, depending upon the virulence of the organism, without producing peritonitis, and that the pathways whereby these are eliminated are as just mentioned, that is, toward the central tendon of the diaphragm and thence to the mediastinal lymph glands.

Now, what I believe is that what is true as regards experimental work and acute infections is true also as regards chronic infections; that is, the attempt on the part of the peritoneum to remove certain noxious agents—for instance, the tubercle bacillus, the infective agent of rheumatism and other diseases, probably certain toxic substances—may result in partial or complete success. In the latter instance the peritoneum may be completely rid of the infective agent, which, being carried to the mediastinal lymph vessels and lymph glands may infect the pericardium or the pleura, giving rise to a primary pleuritis or pericarditis. Subsequently the peritoneum may become infected. In other cases the attempt on the part of the peritoneum to remove the infective agent being only partially successful, the region about the liver and the under surface of the diaphragm succumbs, and a primary perihepatitis occurs. Subsequently the infective agent may travel through the diaphragm and infect the pericardium, or the pleura, or both. In these cases, on account of the peculiar lymphatic supply of the surface of the liver and the under surface of the diaphragm, the infective agent being as it were concentrated to the region about the liver, especially to the neighborhood of the suspensory ligament toward which many of the lymphatics converge, gives rise to the excessive and often hyperplastic lesions sometimes observed. The peculiarities of course and of distribution of the lymphatics of this region are also accountable

for the much greater involvement of the upper surface of the liver (as contrasted with the lower surface) that is present in most of the cases. In this class of cases the primary infection of the peritoneum may be hematogenic in origin ; or it may be of more local source, such as the intestinal tract or the urinary organs ; or, in the case of women, it may result from some genital infection, as appears to have been the fact in Caporali's case. In a number of cases, on the other hand, a primary pericarditis occurs independently of peritoneal infection. Many of these cases are tuberculous in nature—the result generally of extension of disease from tuberculous mediastinal or peribronchial lymph glands, a subject recently discussed at length by Riesman. Following such initial infection of the pericardium the other serous membranes may become implicated in the diseased process. Thus either an ascending or a descending infection of the several serous membranes may occur ; and there is no reason for not believing that in some cases all the serous membranes may become infected at the same time by the same infective agent.

The condition of the liver in these cases now demands consideration. In assigning to the liver a rôle in the production of the ascites we have to bear in mind that in 31 of the cases tabulated chronic peritonitis or chronic perihepatitis or both were present. (There is no note with regard to the condition of the liver in 1 case.) Thus in 31 of the cases the ascites may be accounted for without reference to the condition of the liver substance. In the 7 cases in which there is no note of perihepatitis or peritonitis the liver is described as nutmeg or cirrhotic, or both. In the case of cirrhosis (Feierabend) the ascites may be attributed to the cirrhosis, which may have been an independent affection or the consequence of the long-standing congestion. With regard to the remaining 6 cases—1 of Mott's showed recent inflammatory lymph in the peritoneum, Broadbent's showed recent miliary tuberculosis, whereas the reports of the other 4 cases (Mott, Cantu, Pick, and Cabot) contain no statement whatever with regard to the condition of the peritoneum.

In the absence of statements to the contrary, assuming that the peritoneum was normal in these cases, the cases in which one has to invoke the activity of the liver alone to explain the occurrence of the ascites are still very few. In the majority of cases the ascites is satisfactorily explained by the perihepatitis and the peritonitis, and this fact has to be borne in mind by those that would assign predominance to the liver in the causation of the ascites.

Again, the condition of the liver in the majority of these cases is scarcely that which we usually associate with the production of ascites. In the cases in which the liver was normal aside from compression, as well as in the cases in which there appeared to be only extension of connective tissue from the thickened capsule into the substance of the

organ, predominance in the production of the ascites cannot be ascribed to the liver. Even with regard to the cases in which, in addition to the perihepatitis, cirrhosis of the liver was present, we have to bear in mind that the ascites, in most of the cases, was present at a time when clinically the liver was normal in size or enlarged and presumably not cirrhotic. With regard to the cases in which the liver was large and firm or nutmeg in appearance we have to bear in mind that most of the livers that were subjected to careful microscopic study revealed, as a rule, only varying degrees of chronic congestion and its consequences, and that in many cases the entire absence of periportal connective tissue proliferation has been emphasized. In some of the other cases the connective tissue proliferation although present has been inconspicuous—certainly in most of the cases insufficient alone to account for the ascites, a subject discussed in detail by Eisenmenger. Contrary to the opinion held by Pick and others, therefore, I believe that in the majority of cases primary importance in the production of the ascites cannot be assigned to the liver. However, that the condition of the liver may be a contributing factor in the causation of the ascites, and in the increase of an ascites produced by the serositis (perihepatitis or peritonitis), as for instance, in cases of associated cirrhosis, etc., must be conceded ; that in a few cases the ascites may be brought about in the manner maintained by Pick, that is, as a direct result of the congestion of the liver, may also be conceded. These, which are rare cases, may be likened to the unusual cases of valvular disease of the heart in which disproportionate ascites occurs. Still, it is important to bear in mind that these two classes of cases differ in this respect—that an isolated ascites, such as was present for a long time in many of the cases herewith tabulated, rarely if ever occurs in valvular disease of the heart. In both disproportionate ascites is not uncommon ; in valvular disease of the heart, however, the disproportionate ascites is accompanied by more or less œdema of the extremities, as well as of the trunk—an association that is not uncommon in certain cases of obliterative pericarditis. Under such circumstances the differential diagnosis between these two conditions is a matter of extreme difficulty, if not of impossibility — a subject recently discussed in detail by Türk.

At present, however, I am concerned not so much with this class of cases as with that class in which for a long time isolated ascites is the striking clinical feature. I am inclined to concur with Rosenbach, who states that in these cases the ascites must be the result of the operation of special conditions which although associated with the heart (or pericardial) disease are not the direct result of diminution of the power of the heart and of consequent congestion. While it is probable that all the cases that present the complex of obliterative pericarditis and

ascites may not be of the same nature, I should like to emphasize the importance of the perihepatitis and the peritonitis in the causation of the ascites.

In this connection I cannot forbear to refer to some extremely interesting observations made some years ago by Hale White. This writer, basing his remarks upon 34 cases of cirrhosis of the liver, stated that he was not able to find the report of a single case of uncomplicated cirrhosis of the liver in which the patient long survived paracentesis of the abdomen, that not one patient lived long enough for paracentesis to become necessary a second time, and that many patients died before it became necessary at all. Referring then to a group of 10 cases that had been regarded as cases of cirrhosis of the liver but in which paracentesis had been performed more than once, he concluded: That the supervention of ascites in uncomplicated cirrhosis of the liver means that the end is near; that if a patient with ascites and cirrhosis of the liver lives long enough to require a second paracentesis, it is in the highest degree probable that either the diagnosis is incorrect or that some cause other than cirrhosis exists to explain the ascites; and that such cases nearly always turn out to be examples of chronic peritonitis, with perihepatitis, which is not a special disease but merely a part of chronic peritonitis. I cite these observations merely to emphasize the relative unimportance of the liver in the causation of an ascites that persists as long as, and necessitates as many tappings as, does the ascites in the cases at present under discussion. That recurring ascites occurs in the absence of congestive alterations in the liver is well illustrated also by the case reported by Hübler. In this case, as well as in a number of cases reported by Hale White and others, the serous membrane disease was confined to the peritoneum. Clinically these cases were the counterpart of many of the cases herewith tabulated, but at the necropsy the pleuræ and the pericardium were found intact. There was absence of congestive alterations in the liver, absence of connective tissue hyperplasia in the liver, but there were marked hyperplastic perihepatitis (zuckergussleber) and recurring ascites.

To RECAPITULATE: In a certain proportion of cases of chronic obliterative pericarditis ascites is the striking clinical symptom, and leads usually to the diagnosis of cirrhosis of the liver—whence the somewhat unhappy designation "pericarditic pseudocirrhosis of the liver," suggested by Pick, is not altogether inappropriate. Anatomically the distinguishing feature of these cases is a chronic fibrous (usually hyperplastic) inflammation of the several serous membranes of the body—a multiple serositis. In some cases the inflammation may remain localized to one or two serous membranes, but there exists a marked tendency for all the serous membranes to become involved. The several serous membranes may become involved equally or unequally; usually the

lesions are most marked in the pericardium and on both sides of the diaphragm. In some cases extensive calcification of the pericardium occurs—the case herewith reported being the most marked example of this condition that I have ever encountered. In cases in which there is but partial obliteration of the pleural or the pericardial sacs there is usually also some fluid present. In many cases, however, not only is the pericardium thickened and obliterated, but it has also formed adhesions with the chest wall and the structures of the mediastinum, one or both pleuræ are thickened and obliterated, and the peritoneum is more or less thickened and adherent and contains a large quantity of fluid. In many cases the liver is adherent not only to the under surface of the diaphragm, but also to the stomach, the colon, the omentum, the anterior abdominal wall, etc. The lesions involve also the spleen, especially in those cases in which there are extensive adhesions in the left pleura. A distinguishing feature of the lesions is the development of thick fibrous, almost cartilaginous masses of connective tissue, that encase, compress, and often distort the organs, and give rise to an appearance suggesting confectioners' icing—whence the designation "iced liver" (zuckergussleber). In many cases of primary pericarditis the liver is enlarged, smooth, and has sharp edges; later with the development of the perihepatitis, the liver lessens in size, its surface becomes somewhat irregular, its edges rounded, and sometimes the entire organ becomes much distorted; still later or in some cases earlier the appearances characterized as nutmeg, with or without atrophic alterations, may supervene. Although some slight connective tissue proliferation and some extension of newly formed connective tissue from the thickened capsule sometimes occur, the common absence of marked connective tissue proliferation in the liver is noteworthy. In some cases the lesions of cirrhosis are encountered.

As already stated, the striking clinical feature of the disease is ascites, which is present whether the pericardial and pleural changes are absent, whether they are slight, or whether they are marked. However, the interpretation of the phenomena of the disease is much facilitated by recognizing that taken as a whole—from the beginning to the end—the symptom complex is made up of symptoms due to the serositis and of symptoms due to the disturbances or failure of the circulation induced by the pericardial part of the serositis. As a matter of fact, aside from the ascites, which occurs early, and may be the only symptom for many years, the symptoms are due almost entirely, if not entirely, to failing cardiac compensation. Expressing my own opinion, I should say that there can be little doubt that presenting the complex of obliterative pericarditis and ascites, there are grouped a number of cases that differ more or less in nature the one from the other. However, I believe that

in the majority of cases the ascites is due primarily to the peritonitis and the perihepatitis; that in consequence of the inflammation, the peritoneum becomes a locus minoris resistentiæ; that in consequence of the chronic pericarditis—in reality the pancarditis—the functional activity of the myocardium is interfered with; that in consequence of the lessening of the functional activity of the myocardium the circulation of the blood is more or less impeded—in some cases insensibly impeded; that the region that first manifests the sensible evidences of impeded circulation is the locus minoris resistentiæ—the peritoneum; that the relief afforded the general venous circulation by the accumulation of the ascites, probably indirectly, prevents to some extent the occurrence of œdema of the extremities; that the connective tissue hyperplasia of the liver in some of the cases is due to the same causes that induce the serous membrane inflammation—the irritant being carried by the lymphatics into the liver substance from the diseased capsule; and that in different cases the ascites is increased by the contraction of the newly formed connective tissue of the capsule, by the concomitant peritonitis in the transverse fissure of the liver should it compress the vessels (which occurs rarely if at all), by the marked congestion and its consequences, by concurrent cirrhosis (which is unusual), and by the general failure of the circulation toward the close of life.

Thus, although the disease is characterized by slow, insidious, and intermittent course, the perihepatitis and the peritonitis dominate the clinical picture of the well-developed disease. Aside from this, that is, aside from the ascites, the clinical picture varies, depending upon the point of origin of the disease. In some cases the disease is ushered in with acute pericarditis, pleuritis (which may necessitate repeated tappings), or perihepatitis (circumscribed peritonitis), which subsides and leaves the patient apparently well for a number of years. Usually, however, the lesions of the pericardium and of the pleuræ are latent, and the first sensible evidence of the disease is ascites. In some cases of primary pericarditis slight and transient œdema of the legs may be present clearly, but this is not observed in many cases, inasmuch as the pericarditis is usually latent. When œdema does occur early it usually soon subsides and does not recur until the ascites has been present for a long time or until shortly before death. Except shortly before death it is inconspicuous when contrasted with the excessive ascites. (Reference is not made in this communication to that class of cases in which general failure of the circulation occurs early and in which œdema and ascites develop pari passu.) Associated with early œdema, slight swelling of the spleen and disturbances of the gastro-intestinal tract may develop, but these usually subside with the ascites, and the disease, as a rule, is characterized by the entire absence of such symptoms until

shortly before death. The ascites is characterized by the fact that it is excessive, that it necessitates repeated tappings, that it recurs rapidly after tapping, and that it may remain stationary (not necessitating tapping) for many years.

In a few cases lesions of the peritoneum appear to be entirely absent, whereas, in other cases they are so slight as to appear inadequate to cause the ascites. These cases may be likened to the similar cases of valvular disease of the heart in which disproportionate ascites is the striking clinical feature. In these cases the ascites is doubtless due directly to the congestion of the liver and its consequences, as maintained by Pick. In some cases both factors—the congestion of the liver and the peritonitis—are operative; in some cases rather the congestion of the liver, in other cases rather the peritonitis. In cases in which the congestion is the major factor we should expect more or less swelling of the spleen and disturbances of the gastro-intestinal tract; in cases in which the serositis is the major factor, we should expect an absence of such symptoms. Some distinction—anatomically, at least—may be drawn between cases in which the lesions are confined to the peritoneum and cases in which the lesions are more wide-spread. The cases in which the pericardium is unaffected reveal no congestive alterations in the liver. Clinically, however, the two classes of cases are very much alike, and the "zuckergussleber" may occur in both.

In the diagnosis of this multiple serositis or of chronic adhesive pericarditis with ascites, especial attention should be directed to the history of a previous attack of acute pericarditis, pleuritis, or perihepatitis; to the early occurrence and subsequent disappearance of the œdema of the legs; to the marked ascites, with little or no œdema of the legs; to the enlarged liver early in the course of the disease (in some cases the liver appears not to have been enlarged), and to the small and distorted, but otherwise smooth liver, in the later stages of the disease; to the absence or very late occurrence of marked enlargement of the spleen; to the tendency to the occurrence of repeated attacks of pain, tenderness, rigidity, and possibly palpable and audible frictions in the right hypochondriac region—attributable to attacks of perihepatitis; to the rapid recurrence of the ascites after tapping, and to the physical signs of adherent pericardium—without which, it may be said, the disease is incapable of diagnosis. In the diagnosis of adherent pericardium most help will be derived from: a weak or absent apex-beat, especially in cases in which there is no increase in the area of cardiac dulness; systolic retraction of a considerable area about the apex; systolic retraction of the base of the left chest posteriorly; arrest of the normal respiratory movements in the epigastric angle; imperfect descent of the apex-beat during inspiration; inadequate or entire absence of

shifting of the apex-beat, with change in the posture (lateral posture) of the patient; absence of change in the limits of the cardiac dulness during the respiratory phases; absence of increase of the cardiac dulness to the right, despite marked engorgement of the veins of the neck; a diastolic shock or rebound of the heart; evidences of dilatation or hypertrophy of the heart in the absence of valvular or other disease that might cause it; absence of the characteristic changes in the heart in the presence of definite valvular disease—that is, absence of the usual hypertrophy of the right ventricle in mitral disease and of the left ventricle in aortic disease; absence of pericardial effusion in the presence of pleural and peritoneal effusions; paradoxic pulse—inspiratory diminution in the force and volume of the pulse; diastolic collapse and inspiratory swelling of the veins of the neck; and, as suggested by Musser, the non-occurrence in young subjects with valvular disease and cardiac insufficiency of the characteristic improvement following the administration of digitalis. None of these is pathognomonic of adherent pericardium; all will not be present in every case; but in many cases a sufficient number may be present to warrant the diagnosis.

Finally, this obliterative pericarditis with ascites may be distinguished from cirrhosis of the liver: by the aforementioned symptoms and signs of adherent pericardium; by the absence of the etiological factors of cirrhosis of the liver; by the slow, insidious, protracted, and intermittent course of the disease; by the long periods of standstill during which the ascites may remain stationary and the patient in good condition; by the entire absence or the transient presence of slight jaundice; by the absence in most cases of portal congestion and gastro-intestinal disturbances—hemorrhage, diarrhœa, hemorrhoids, enlargement of the spleen, marked dilatation of the superficial veins of the abdominal wall, etc.; in some cases, by the association of an enlarged, smooth, and firm liver, with marked ascites; and by the fact that in many cases the patient survives a large number of tappings.

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NOTE.—Since the foregoing paper was read the following articles have come to hand: Becker: Obliterative Pericarditis, with Hepatic Enlargement and Ascites. Philadelphia Medical Journal, March 25, 1902, vol. ix. p. 485; Simon: Zur Kenntnis der Zuckergussleber. Inaug.-Diss., Königsberg, 1900; Centralblatt für innere Medicin, 1902, vol. xxiii. p. 491; Pfannkuche: Zur Kenntnis der serösen Peritonitis und der Perihepatitis im Zusammenhang mit Perikarditis und Pleuritis. Inaug.-Diss., Kiel, 1901; Centralblatt für innere Medicin., 1902, vol. xxiii. p. 515; Strajesko: Ein Fall von Pseudocirrhose der Leber. Allgemeine Wiener medizinische Zeitung, 1902, vol. xlvii. p. 60; and Nicholls: On a Somewhat Rare Form of Chronic Inflammation of the Serous Membranes (Multiple Progressive Hyaloserositis). Studies from the Royal Victoria Hospital, Montreal, 1902, vol. i. No. 3. The article by Nicholls, which deals especially with the pathologic-anatomic features of chronic inflammation of the serous membrane, is the most exhaustive and comprehensive discussion of the subject that has yet appeared in the English language.

REVIEWS.

AMERICAN EDITION OF NOTHNAGEL'S ENCYCLOPÆDIA OF PRACTICAL MEDICINE. TYPHOID FEVER AND TYPHUS FEVER. By DR. H. CURSCHMANN. Edited, with additions, by WILLIAM OSLER, M.D. Authorized translation from the German, under the editorial supervision of ALFRED STENGEL, M.D. Philadelphia and London: W. B. Saunders & Co., 1901.

THE appearance of the first volume of the authorized American translation of *Nothnagel's Encyclopædia of Practical Medicine* should be hailed with sincere pleasure by the entire profession of this country. The work in the original has long been familiar as a standard authority to those who had access to large libraries, and to them has proved of inestimable value. The publishers have undertaken an enterprise in which they should be supported by all those who are interested in the progress of scientific medicine in this country.

The present volume has been edited with additions by Osler, and it is needless to say that under his supervision the work has assumed a value beyond even that of the original.

The portion of the book devoted to the subject of typhoid fever is naturally much larger than that given to typhus fever, and most of the changes and additions made by the American editor have been to this part of the work. These changes, as stated in the preface, have consisted chiefly in the incorporation within the text of the important results of the investigations by Mallory and Thayer and other American workers.

The consideration of typhoid fever is divided into etiology, pathology, diagnosis, prophylaxis, and treatment. The section on Etiology begins with an admirable historical sketch which represents a type of the progress made in our study and knowledge of disease by modern methods; it is followed by several sections dealing with our knowledge of the nature and properties of the typhoid bacillus, including the subject of infection, and closing with a most apt summary of the conclusions to be drawn from the most recent investigation.

The pathology of the disease, its symptoms and complications, are dealt with at great length. The section on Diagnosis deals with the subject from the point of clinical investigation and from that of bacteriological study. It begins with the statement that "The ideal method of diagnosis of typhoid fever would be the demonstration, with readiness, rapidity, and certainty of its cause, the bacillus of Eberth during every period of the disease," and this statement is undoubtedly true, but as we find emphasized further on, "At present observation at the bedside still retains the first place in diagnosis."

In the section on Prophylaxis we find the topic divided into a discussion of general measures, special individual measures, and preventive

inoculation. Of the latter, it is stated that so far experience is strongly in its favor, although it must stand the test of wider application.

The section on Treatment is very complete. The serum treatment, it is shown, has not as yet proved of much efficacy, and the same may be said of the antiseptic method. The principal factors in the treatment are stated to be the appropriate care and regulation of the condition of the patient, especially in a dietetic direction, and in the treatment of important symptoms, complications, and accidents as they may arise.

Of that portion of the book devoted to typhus fever, the same general statements may be made as regards the first division. The disease has been considered under the same headings and in the same lucid and complete manner that typhoid fever is written of. Typhus fever is so rarely seen by the practitioner that there must be a strong temptation to slur over some of the features of the disease in writing of it. No such lack of care is evident in the present description, and it has the advantage of being written by men who have seen and handled the disease in question.

Particular attention should be directed to the admirable manner in which the work of translating and re-writing has been performed. We have but rarely perused a medical work in which the language was more elegant, or which read with greater ease. We have only to add that should the rest of the volumes prove as excellent in every respect as the one under consideration, the enterprise will be worthy of all possible success. F. A. P.

The Principles and Practice of Gynecology, for Students and Practitioners. By E. C. Dudley, A.M., M.D., Professor of Gynecology, Southwestern University Medical School; Gynecologist to St. Luke's and Wesley Hospitals, Chicago, etc. Third edition, revised and enlarged, with 474 illustrations, of which 60 are in colors and 22 full-page plates in colors and monochrome. Pp. 761. Philadelphia and New York: Lea Brothers & Co., 1902.

From the author's statement in the preface, the reader will infer that, while the original plan of the book has been preserved, radical changes have been made in this edition, and much new matter has been added. One accordingly feels that it is incumbent upon the reviewer to bestow more careful attention upon it than is indicated by the usual perfunctory notice of the latest issue of a successful text-book. Having already presented an extended general review, we shall confine ourselves principally to the new features mentioned by the author. In the new paragraph on the anatomy of menstruation he accepts unhesitatingly Gebhard's view that there is no shedding of surface epithelium during the process. Chapter XV., on Endocervicitis, seems to have received more attention than its relatively slight importance merits. We have always thought that there was no advantage in treating it as a separate disease. Schroeder's operation is so rarely performed at the present time, as compared with amputation of the cervix, that it might well have been omitted. The chapter on Chronic Endometritis has been carefully worked over, especially the section on Curettage, in which there are several excellent new illustrations (Figs. 151 to 156, inclusive). We shall not renew our objection to the author's infective theory, with

which we are not entirely in accord. The present arrangement of the points in differential pathology and diagnosis (which, by the way, is borrowed from Thomas) is a decided improvement here and elsewhere throughout the book. We are a little disappointed to find that chronic metritis is still retained as a separate entity, as it is an "end-process" rather than an inflammatory condition. The explanation that the term is "taken in its broader sense," so as to include even perimetritis, will not render it less objectionable to some more critical readers.

The author manfully champions the cause of cellulitis, and we admire his conservatism even when it leads him to introduce the time-worn parallelism between cellulitis and peritonitis. We shall not enter into a fresh controversy with him regarding the pathology of pelvic inflammation, as his treatment is sound. Chapter XXIII., on the Surgical Treatment of Salpingitis, Ovaritis, and Pelvic Peritonitis, is fully abreast of the times, and shows the author at his best.

The chapters on Fibromyoma and Cancer have been carefully revised and enriched with numerous plates of unusual artistic beauty and practical value (especially VIII. to XIV., inclusive). The author's method of securing the stumps after abdominal hysterectomy, with which we are already familiar, is carefully described and figured—possibly at too much length for a text-book. The same criticism might be applied to the technique of vaginal hysterectomy for cancer. Of the radical abdominal operation he thinks so poorly that he dismisses it with a few lines.

Although it is stated that the chapter on the Pathology of Ovarian Tumors has been rewritten, we still feel that it has not received the attention which its importance warrants. This criticism does not apply, however, to the succeeding chapters on Symptomatology and Differential Diagnosis, and on Ovariotomy. In the latter chapter (XXXIV.) the reader's attention will be at once arrested by the admirable plates (XVII.–XIX.), which are literally in a class by themselves. Tubal pregnancy has been definitely adopted by modern writers as a gynecic rather than an obstetric condition—a surgical fact and not a pathologic curiosity. The author treats it thus, and in the most approved way.

It is unnecessary to repeat our former praise of the chapters on Plastic Surgery. Here, in his descriptions, as in his own work, the author is *facile princeps*. We honor him none the less that among all the changes and innovations of the age he is faithful to his purpose not "to remove the ancient landmarks which the fathers have set up." Doubtless the typical Emmet operation for lacerated cervix will be generally replaced by amputation when any operation seems to be indicated, but it will be long before American gynecologists, of this generation at least, will hold in light esteem the work of that great teacher. Lack of space prevents our noting the changes and additions under the head of Uterine Displacements. We can only say that they seem to render still more readable and instructive these excellent chapters.

After all, Dudley's *Gynecology* needs no fresh encomiums. The best proof of the inherent value of a medical work is afforded by its instant and wide popularity and by the appearance in rapid succession of new editions. Many men would be content to rest on their laurels. Not so our friend the author, who always seeks to give us his best. Surely his hope expressed in the dedication has been realized. He is indeed a "worthy pupil" of his beloved teacher. H. C. C.

BERICHT UEBER DIE VON KOMITEE FUER KREBSFORSCHUNG AM 15 OKTOBER, 1900, ERHOBENE SAMELFORSCHUNG.

REPORT ON THE COLLECTIVE INVESTIGATION MADE BY THE COMMITTEE FOR THE INVESTIGATION OF CANCER. Edited by the Directors, PROFESSORS VON LEYDEN, KIRCHNER, VON HANSEMANN and MEYER, and DR. WUTZDORFF. Supplement to the *Klinisches Jahrbuch*. Jena: Gustav Fischer, 1902.

THE work before us is the first result of a formal attack upon the cancer problem by the medical profession and Government of Germany. Under the initiative of Professor von Leyden a committee was formed in 1900 to foster investigations, and a census of cases under observation on a given day was planned. This was materially furthered by the government, including the Imperial Health Bureau. Cards and directions were sent to more than 25,000 physicians and institutions, and over 12,000 cards available for the census were returned. Although there were many faulty answers, it seems probable that most of the cases known to physicians were reported, so that the material studied forms an imposing mass. While the results to be expected from such an investigation are limited, they cannot but be of interest; and although the tabular form of the report, covering as it does a great array of material, does not lend itself to brief review, it is possible to give some conclusions. It should be said that the present collective investigation is only one of several projects of the committee. Various studies of special topics are now under way. Czerny and Mommsen, for example, are ascertaining the time which elapses after successful operations (on cancer of the breast) before recidive, a period which may have some relation to the latent stage of the primary attack. A number of lectures on certain aspects of cancer have been given in Berlin under the auspices of the committee, but the most promising outcome of its work is the foundation of two institutes for the investigation of cancer—one in Professor von Leyden's clinic, the other in Professor Ehrlich's Institute for Experimental Therapy, in Frankfort. Among the points of interest brought out in the work under review are the following: Cancer generally occurs more frequently in cities than in the country, though there are local exceptions. It is more common in women in cities and in men in the country, also with local exceptions. There are many differences in the morbidity of adjacent places. So in Berlin the proportion is 319 per million; in Charlottenburg, 275; in Rixdorf, 133; in Hamburg, 362; but in Altona, 235. Several industrial towns have very low proportion, as Bochum, with 46 per million. As regards the proportion of women and men, there are many factors, such as age, that have to be still further investigated. Considerable attention was paid to the existence of cancer foci, and some suggestive facts were elicited, but much remains to be discovered. The investigation shows, as has long been known, that cancer is rare in the first two decades of life. The increase begins earlier in women and the decline later. The period of greatest morbidity in women is seventy to eighty years; in men, sixty to seventy years. The latter decade is the only one in which there are more men affected than women. These differences depend on the frequency of cancer in the female breasts and genital organs. Of 1000 cancerous women between fifteen and thirty years of age, the organs mentioned are concerned in 644; between thirty and forty, 746; between seventy and eighty, 374. In men a similar preponderance is

seen on the part of the digestive tract. This part of the investigation contains many details as to the seat that can only be referred to here. A curious fact is that men in cities are more disposed to cancer of the digestive tract than those in the country. Other interesting facts in this connection are the frequency of cancer of the skin in country people and in washer-women, and cancer of the respiratory organs in metal workers. The question whether cancer is increasing is shown by the Prussian statistics to require an affirmative answer. The increase from year to year is so even that accident and error can be excluded. Dr. Wutzdorf has shown in one of the lectures alluded to (*Deutsche med. Wochenschrift*, No. 10, 1902) that the increase of cancer is out of proportion to the increase of population. The idea sometimes advanced that the increase can be explained by the greater average age now reached is not confirmed by figures. On the other hand, cancer shows a tendency to occur earlier than formerly, and is increasing more rapidly in men than in women. The investigation does not tend to prove the idea of the inheritance of cancer in the old and still commonly used sense. Of the men patients, the mothers were affected in 4.3 per cent., the fathers in 4.7 per cent. Of the women, the parents were affected in 7.2 and 3.1 per cent. respectively. As in the case of tuberculosis, there are many examples of a family tendency. Infection was believed to have occurred in 3.6 per cent. of all cases. Two hundred and eighty cases concern husband or wife, 20 the parents, and 135 other people; 5.2 per cent. besides those just mentioned lived with or near other cases of cancer. The report points out that this question is one to which practitioners should pay special attention.

From the details given it may be seen that the report is in many respects a model. In mode of execution the work planned cannot be easily imitated in other countries. But the present report gives large series of figures in connection with many unsettled problems concerning cancer, and points out many lines of investigation that can be taken up in various places. It will therefore be studied with gratitude by all who try to discover the nature of one of the most important diseases that "still baffle the scientific and medical world." The volume includes the report of the Netherlands Commission on Cancer, the results of which correspond closely with the larger ones obtained by the German committee. Three tinted maps show the geographic relations of cancer in general, and in men and women separately. G. D.

AMERICAN EDITION OF NOTHNAGEL'S ENCYCLOPÆDIA. DIPHTHERIA, MEASLES, SCARLET FEVER, AND GERMAN MEASLES. Diphtheria. By WM. P. NORTHRUP, M.D., of New York. Measles, Scarlet Fever, and German Measles. By PROFESSOR DR. TH. VON JURGENSEN, Professor of Medicine in the University of Tubingen. Edited, with additions, by WILLIAM P. NORTHRUP, M.D., Professor of Pediatrics in the University and Bellevue Medical College, New York. Octavo, 672 pages, illustrated, including 24 full-page plates, 3 of them in colors. Philadelphia and London: W. B. Saunders & Co., 1902.

A WORK as well known as Nothnagel's *Encyclopædia* needs no introduction to the medical profession. Its established reputation as a repository of medical knowledge has long since made it an often consulted

work on the shelf of the practitioner. The third volume of the American edition has just appeared.

The first article, on Diphtheria, written by Dr. William P. Northrup, is a masterly exposition of this disease under well classified headings. It is an exhaustive treatise on the subject brought up to date, containing many interesting statistics and numerous instructive charts. The article is concluded by a long and detailed account of the operation of intubation, beginning with an account of O'Dwyer's earliest attempts at this procedure, and gradually tracing the development of the intubation tube up to the most approved pattern as now made. The value of this section is much enhanced by a series of X-ray photographs showing the anatomical relations of the operation.

The remaining articles in this volume by Professor von Jurgensen are preceded by an interesting discussion on the infectious exanthemata in general, which indorses von Kerchensteiner's views regarding quarantine, and propounds a doctrine widely at variance with the board-of-health rules as practised in this country. The admirable article on Measles contains a very thorough consideration of the pathology of this disease, much of its value being derived from a careful study of the Danish records of the Faroe Islands epidemic.

Quite up to the high standing of the preceding chapter is the treatise on Scarlatina, which gives special care to the study of its etiology and pathology, and shows a very just and unbiased weighing of the recorded literature on the subject.

The treatment of Scarlet Fever as advocated will perhaps seem too radical to some practitioners; but we are rapidly passing beyond the belief that the sequential nephritis is due to "catching cold," as formerly taught, or that pneumonia in fever patients is produced by draughts or insufficient bedclothes.

By way of criticism, we might object in some instances to the too liberal translation of some German idioms. But, as the work is not published as an exposition of English rhetoric, the fault is a minor one.

The volume ends with a short consideration of Rubeola and the Fourth Disease. It contains throughout many charts, and has been rendered more valuable to the American reader through appropriate additions by the editor. G. W. N.

Reynolds and Newell's Practical Midwifery. A Manual of Obstetrics for Students and Physicians. By Edward Reynolds, M.D., Assistant in Obstetrics, etc., and Franklin S. Newell, M.D., Assistant in Obstetrics and Gynecology in Harvard University Medical School, Boston. In one octavo volume of 531 pages, with 253 engravings and 3 full-page colored plates. Philadelphia and New York: Lea Brothers & Co., 1902.

In their preface the authors assert that any medical book of the present day must needs show reason for its existence. With this view we are in hearty accord, and it gives us great pleasure to be able to say that the present volume meets the requirements of its authors. Naturally, there is nothing new and startling, since in obstetrics, as well as in gynecology, we have reached, as it were, level ground, where—as even the medical societies show—we are all more or less in accord, and where

—for the present at least—the acrimonious discussions of a decade ago are impossible.

But what this book does is to present, in a very clear, practical manner the generally accepted teaching, as modified by the experience of the authors. The work, indeed, bears the unmistakable hall-mark of the authors' practical experience. It is not intended as an exhaustive reference-book, but as a practical treatise for the use of the busy man.

There is much to praise and but little to censure. Of special value are the chapters on delayed labor and on high arrest of the posterior occiput. The section devoted to the consideration of pelvic deformities is also well written and full enough to answer its purpose. The major obstetric procedures receive requisite space, and, in a word, the whole book is well balanced.

To our mind the most important criticism is that the use of rubber gloves is not forcibly advised as a routine measure in delivery. It is certain that no man is justified in attending a woman in childbirth without taking this precaution, if he be at all doubtful of his personal asepsis; and we feel that it is equally certain that the ordinary obstetrician—viz., the general practitioner—can never assume that he is surgically clean.

The only other adverse criticism that we would make is that in the discussion of placenta prævia more space should have been given to the question of diagnosis. W. R. N.

A Text-book of Diseases of the Ear. For Students and Practitioners. By Professor Dr. Adam Politzer, of Vienna. Translated at the personal request of the author, and edited by Milton J. Ballin, Ph.B., M.D., and Clarence L. Heller, M.D. Fourth edition, revised and enlarged. Philadelphia and New York: Lea Brothers & Co., 1903.

The publication of a new English edition of this work which stands in a class absolutely by itself as the most complete exposition of the science of otology by its foremost living exponent is a matter of great importance to all physicians especially interested in that subject in this country. It is given to but few books to attain the position of absolute authority which is universally conceded to Professor Politzer's work. Few men have done more than he to bring about the advances in otology which have necessitated the issuance of a new edition of this standard volume. The present edition is larger than the last, and many things which were under dispute at the time that edition was published are now relegated to the position which they should occupy.

A notable feature of the book, and one which is so often lacking from German text-books, is to be found in what one may term its universalism. Not only is the work of German scientists and physicians considered, but due credit is given, *mirabile dictu*, to the work of American otologists such as Knapp, Burnett, Randall, Roosa, and Blake. Most of the work has been entirely rewritten, and all of it thoroughly revised and brought up to date. There are many minor changes in the arrangement, but all of them for the better. Thus the section on otosclerosis, which has replaced that on chronic dry middle-ear catarrh, is entirely recast, and many important results of recent investigation given in an easily accessible form.

Professor Politzer is strongly opposed to operative measures in the treatment of otosclerosis, and thinks we are just as powerless in this condition as we have ever been. The section which deals with operative procedures upon the mastoid process has been enlarged and rewritten, and as it stands now is the most authoritative and up-to-date description of the various methods employed with which we have met.

In no portion of the book do we see greater evidences of scientific advance in otology than in the section which deals with intracranial diseases of otitic origin. It is practically a new section, and it is of the greatest value. Another addition to the work is an appendix containing the prescriptions most commonly used at Professor Politzer's clinic. These prescriptions are, of course, of great value, but their usefulness would be greatly enhanced if they were not written in the metric system. The time has not yet come when the American practitioner can avail himself of this method. It is a pity that the English equivalents were not given in the prescriptions.

The present edition of Politzer is indeed an old friend in a very new dress. The translation is entirely new, having been undertaken by two gentlemen who had been working as voluntary assistants with Professor Politzer for some years, and it is a vast improvement over that used in the previous editions. The typography and the illustrations in the present edition are also much more satisfactory than that of the last. We can only repeat that there is no work in any branch of medicine or surgery which occupies the unique position of Politzer's *Text-book of Diseases of the Ear*. It is an absolute *sine qua non* for the practitioner who devotes special attention to otology or rhinology, and should be in the library of every physician as a book of reference upon these topics. F. R. P.

THE PHYSICIAN'S VISITING LIST FOR 1903 (Lindsay & Blakiston). Philadelphia: P. Blakiston's Son & Co.

THIS *Visiting List* now in its fifty-second year of publication, is one of the most useful books of its class. It presents the usual accompanying letter-press on various matters of practical value to the practitioner, and continues to merit the favor with which it has always been received. R. M. G.

THE MEDICAL NEWS VISITING LIST FOR 1903. Philadelphia and New York: Lea Brothers & Co.

THIS well-known *Visiting List* is published in four different styles: Weekly, dated, for 30 patients; monthly, undated, for 120 patients per month; perpetual, undated, for 30 patients weekly and 60 patients undated.

The arrangement of its record pages is very simple and practicable. The book is strongly made and bound, and contains pages adapted for all the various data which prove of value to the physician in his daily work. It is accompanied by extensive tables of weights and measures, with information of value in various emergencies which may arise, such as poisons and their antidotes, the ligation points for the arteries, how to perform artificial respiration, etc. G. M. C.

PROGRESS

OF

MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF

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Persistent Hereditary Œdema of the Lower Limbs.—ROLLESTON (*The Lancet* September 20, 1902, p. 805) has observed a very interesting form of persistent œdema in three members of one family. The mother, aged forty-five years, had suffered from the œdema for thirty-five years. The condition had existed in a daughter, aged sixteen years, since she was thirteen years old. A son, aged thirteen years, had had the œdema since the age of ten.

The œdema was permanent as long as the individual led an ordinary life, became more marked after exercise or a warm bath, but disappeared after rest in bed for some days. In all cases it was only troublesome from the weight and size of the swollen legs. There was evidence of enfeebled circulation in all three cases. In the mother's case pressure on the skin would leave an anæmic area for a much longer time than in normal persons. The boy and girl were both "blue children" at birth and were subject to chilblains, both the feet and hands getting livid by cold. The œdema in all cases was painless. It was permanent, and did not come on suddenly as in angioneurotic œdema. The heart, urine, and blood were normal in all three patients. The only effective treatment was rest for days in the recumbent posture. This relief was only temporary.

Rolleston states that the cases appear to resemble the remarkable family described by Milroy, of Omaha, in which out of 97 individuals in six generations, 22 persons (12 males, 7 females, and three of unknown sex) had solid œdema of one or both legs without any special inconvenience or progressive increase in the disease. In these cases the œdema was congenital, except in one instance, whereas Rolleston's cases were hereditary and developed from the tenth to the thirteenth year. Rolleston states that the disease in some respects resembles both Raynaud's disease and erythromelalgia, but differs

from both in essential features. He suggests that this peculiar œdema from gravitation may depend on some inherent defect or peculiarity of the small bloodvessels, which allows excessive transudation to occur on very slight provocation. The cases are reported to call attention to the occurrence of cases of œdema not due to the usual causes and which are hereditary and may be congenital.

The Presence of the Widal Reaction in Weil's Disease.—Eckardt (*Münch. med. Wochenschr.*, 1902, xlix. p. 1129) reports two interesting cases of Weil's disease, in each of which the blood serum showed a strong Widal reaction. The first case was that of a young man, aged twenty-two years, whose illness began suddenly with chills, fever, and general prostration. After several days the fever began to diminish, but severe nose-bleeds occurred, while jaundice and an acute hemorrhagic nephritis set in. On the seventh day on entering the hospital the patient appeared very ill and complained of severe pain in the calves; the tongue was dry and coated; the spleen palpable. The patient soon improved subjectively, and the fever disappeared on the following day, but the jaundice and splenic enlargement continued for over two weeks. On the tenth day of the disease the Widal reaction was tried; this resulted in a positive reaction in a quarter of an hour at a dilution of 1/100; in two hours at 1/1000. It was discovered that the room-mate of this patient had passed through a similar illness about a month before. This case was also investigated, the serum showing an agglutination in three-quarters of an hour at 1/50; in an hour and a half at 1/100, and a partial agglutination in two hours and a quarter at 1/1000.

Grünbaum and the author have both noted that the blood of jaundiced individuals has almost always a considerable agglutinative power with cultures of the typhoid bacillus, while the fresh bile, from the same case perhaps, appears to have no such effect. The agglutinative power in the blood serum of these two cases was, however, stronger than has ever been observed in jaundice, while in six other cases it persisted after the jaundice had disappeared. There were also features in the case observed clinically which were not unlike those of an abortive typhoid fever. If the blood serum in jaundice has this agglutinative effect, then, the author suggests, it might well act as a protection to the organism in cases of existing typhoid infection. This naturally brings up the question as to whether Weil's disease may not, after all, be simply typhoid fever which has been aborted as a result of the development of jaundice. Weil, indeed, in his original article states that the disease may be abortive typhoid, while Fiedler, though opposing this theory, admits its possibility. Haas and Weiss have both noted the coincidence of the frequency of Weil's disease at the height of typhoid epidemics.

Eckardt is guarded in his statement and avoids drawing a hasty conclusion, pointing only to the extremely suggestive character of these observations.

Acute Polymyositis.—Bacialli (*Il Policlinico*, 1902, No. 13, fasc. 1 and 2, 16) reports from Tizzoni's clinic an extremely interesting case of acute polymyositis. The patient was a man, aged thirty-nine years, who, in August, 1899, began to complain of rheumatic pains in the upper part of his trunk,

and especially in the arms, which appeared to be heavy and weak. Eight days later the left arm became swollen, while the general indisposition increased. The swelling soon spread and became diffuse, extending also to the neck, throat, thorax, right arm, and afterward to the legs and feet. These symptoms continued off and on until his entrance into Tizzoni's clinic, in October. At that time the patient was bed-ridden; there was diffuse, subcutaneous œdema, the legs, eyelids, and forehead alone being spared. The mucous membrane of the mouth was greatly injected and œdematous; swallowing was difficult; there was extensive œdema of both upper and lower extremities, of the abdomen, and of the thorax. There was a papular erythema on the back. There was great difficulty in moving the arms and legs. While pressure in the œdematous areas was not painful, yet on deeper palpation severe pain was elicited, clearly due to pressure upon the muscle. The special senses were normal, excepting for slight deafness. The spleen was palpable; nothing remarkable about the reflexes. Reactions to the faradic current were diminished, but elicited by strong currents. The blood showed a slight anæmia; red corpuscles, 3,704,000; hæmoglobin, 75 to 80 per cent.; colorless corpuscles, 5580. The condition remained practically unchanged up to the time of the patient's death. There were at times slight remittent attacks of fever, which rose occasionally to 39½° C., lasting several days. On the 18th of December the patient was suddenly seized with dyspnœa, and died shortly afterward with the phenomena of bulbar asphyxia, due clearly to paralysis of the respiratory muscles. During a febrile period in December a small piece of muscle was removed from the left leg. From the muscle pure cultures of staphylococcus albus were obtained. Similar cocci were seen microscopically in the blood obtained at the point of incision. Pure cultures of the staphylococcus albus were obtained from the heart, liver, and muscle. A centimetre of a twenty-four hours' culture in bouillon injected subcutaneously into a rabbit produced little effect, but a few degrees of fever and no serious impairment of the health of the animal. Microscopically the muscles showed appearances similar to those described by other authors in dermatomyositis. In parts of the muscles there was marked œdema, considerable increase in interstitial connective tissue, with abundant infiltrations of white corpuscles, and here and there extravasations of blood. There were widely distributed inflammatory and degenerative changes in the muscle fibres themselves, of which the author describes three stages:

(1) With considerable increase in the number of the muscle nuclei, while the contractile substance preserved its ordinary structure.

(2) With a light increase in nuclei, while the contractile substance, however, had lost its normal structure, appeared more homogeneous, and was extensively vacuolated.

(3) Where the nuclei, excepting in rare exceptions, were materially diminished in number or have entirely disappeared, while the contractile substance had wholly degenerated into a homogeneous, transparent mass similar to hyaline or waxy material.

These alterations the author attributes to an inflammatory process which has produced in the muscular tissue lesions of various degrees, from simple irritation manifested by a considerable increase in the number of nuclei to much graver lesions, such as degeneration and complete destruction of the

contractile substance. He believes the condition to have been a septico-pyæmia of very gradual course, similar to those which the old authors have called chronic septicæmias.

The muscular lesions are attributed to the effects of toxic products of the staphylococcus albus. The attenuated staphylococcus albus may have entered through the fauces, which from the beginning were markedly affected.

SURGERY.

UNDER THE CHARGE OF

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The Treatment of Testicular Ectopy.—COUDRAY (*Revue de Orthopédie*, January, 1902), after a careful review of the subject, states, in conclusion: 1. The treatment of testicular ectopy—ectopy without hernia—should be commenced early, at the age of two or three years. 2. Before attempting mechanical treatment one should try the thyroid treatment, with a dose of 5 centigrammes a day for those under the age of three, and 10 centigrammes daily for those who are over that age, and the dose in the latter class progressively increased to 15 or 20 centigrammes daily. 3. If two or three months of this treatment gives no appreciable results, then one should have recourse to mechanical reduction by pressure or traction. This should be done for four or five minutes each day. 4. When the testicle is distinctly beneath the ring and the cord slips easily along one should advise the carrying of a bandage like a fork, which has the effect not only of retaining the testicle beneath the external ring, but also prevents the wall guarding the ring against the issue of intestine. This wall is often very feeble in these cases. Experience has shown that the unilateral bandage cannot be well applied in the case of young children. It may be preferable in those cases of unilateral malposition, and this may also apply to the hernia of young children, but the double bandage is to be preferred, as a rule, as it has much more firmness. It is well to wear this bandage two or three years, renewing it whenever necessary. The fixation of the testicle at the bottom of the sac may be a useless manœuvre. The bloodless method has the greatest chance of success in young children and those up to the age of ten or twelve years. In those who are older it seems that its employment favors the development of hernia or hydrocele of the cord. 5. Surgical interference is indicated in those cases where there has been some check in the preceding methods; that is to say, when the cord cannot be drawn out or when the testicle is painful

or uncomfortable. In the cases of inguinal ectopy, one nearly always pulls the testicle out in those children who are well nourished. In the iliac variety, on the contrary, when the testicle is not mobile, it is to be hoped that surgical intervention will permit of its replacement in a normal position. In spite of this, the search for the iliac testicle, when painful, is indicated, and it should be removed if replacement is impossible, for a large number of cases have demonstrated that this retention is a source of danger. In all cases one may do a radical cure; that is to say, the resection of the vagino-peritoneal canal after ligation of the neck of the sac in the abdomen. 6. In those children who are not under proper surveillance, and who, in consequence, benefit but vaguely by a bandage, the indications are for early operation. 7. One question remains, Are the testicles which are brought down by the bloodless method less exposed to the danger of atrophy than those replaced by operation? Possibly, but the demonstration of the fact still remains to be made.

Resection of Nearly Eight Feet of Gangrenous Intestine; Recovery.—Harris (*Medical Record*, New York, October 11, 1902) states that the removal of large portions of the intestines, with recovery of the patient, is becoming much more common than in former years, and where there is an abundance of time in which to prepare the patient, with plenty of assistance and good light, this operation is robbed of many of its difficulties; but when, on the other hand, the operation is performed in an emergency, after the patient has been brought a long distance in an ambulance, he being more or less exhausted, with a violent peritonitis in progress, it is an entirely different thing. These circumstances, together with the extreme length of the intestine removed and the apparent complete recovery of the patient, are the reasons for reporting the case of a man, aged thirty-three years, whose history was negative except for four attacks of severe abdominal pain during the past five years. The present attack came on suddenly in the morning with severe pain, which centred in the umbilical region. This soon passed off under brandy and massage of the abdomen, and the patient laid down and slept about an hour. On arising the pain began again, and was more severe than at first. A physician was called and two hypodermics, each of one-quarter grain of morphine sulphate, were given without relief. The patient vomited fluid and mucus, and enematas of hot water proved ineffectual. There was a point of tenderness about the size of the palm of the hand above and to the left of the umbilicus. Operation being decided upon, the patient was removed to the hospital in an ambulance, a distance of twelve miles, and arrived there at 1.30 o'clock in the morning. Nothing definite was learned by an examination of the abdomen, and an incision was then made in the right hypochondrium. As soon as the abdomen was opened there was a tremendous gush of blood-stained serum containing blood and lymph, showing that an acute peritonitis was in progress. Exploration with the fingers showed a large mass of intestine, bound down in the right iliac region, so the wound was closed and the abdomen reopened in the median line, when a very large mass of gangrenous intestines appeared. The mass was about seven inches in the transverse diameter, and the coils of which it was composed ran, for the

most part, transversely, a few, however, were parallel with the long diameter of the abdomen. The point of constriction was close to the posterior abdominal wall and the cæcum. It being impossible to uncoil the intestines, the constricting band, which seemed to be mesentery of about the size of a lead pencil, was divided and the intestines spread out on hot towels and allowed to remain for over twenty minutes. The intestine proved to be the ileum; the mesentery in many places was sloughing and entirely gone. There was one spot where a perforation had taken place, but there did not seem to have been much extravasation. The color not having improved, the ileum was clamped and divided close to the cæcum, the remaining vessels of the mesentery were tied and cut away close to the spine; above, the division was made one inch from the upper limit of the gangrene. The mass of gangrenous intestines was then removed, and the abdomen thoroughly flushed out with hot salt solution, and preparation made for joining the intestines. The opening in the cæcum was closed, the edges being inserted and closed with a double row of Lembert sutures, one-half of a Murphy button being first put into the cæcum. This button was then pushed against the wall on the other side of the cæcum beside the appendix, and, an opening being made, the button was brought through and held by an assistant. The end of the ileum was inverted and closed by a double row of Lembert sutures, the second half of the button having been previously placed in the bowel. This was brought through in the same way as the other, and the intestine was joined to the cæcum by a lateral anastomosis. No additional sutures were required except in the mesentery. The abdomen was again thoroughly flushed out, the wound closed in the usual manner, and a wet bichloride dressing applied. The portion of intestine removed measured seven feet ten inches. The patient had two large abscesses in the abdominal wounds during convalescence, one at the first incision and the other at the opening in the median line. These finally closed and the patient left the hospital weighing more than when he entered, and now feels as strong as ever. The Murphy button was found in the rectum on the twenty-fourth day, and removed. In closing, the author gives a list of thirty-five cases in which the length of the resected portion of intestine varies from forty inches in the first case to twelve feet two inches in the last.

Operation for Paralytic Club-foot.—Schanz (*Centralblatt für Chir.*, June 28, 1902), states that paralytic club-foot is usually treated at the present day by first undertaking the correction of the deformity, and then trying, through transplantation of the tendon, to increase the lost function of the peronei. In transplanting one usually secures the best material by incising off a portion of the tendo Achilles. The bloody part of this treatment is really two separate operations—transplantation and lengthening of the tendo Achilles. While both of these operations may be performed at one sitting, as a general rule it will be found better to first do the transplantation, and then, some four or five weeks later, proceed to lengthen the tendon. The reasons for this are: 1. The same reasons as apply to the operation in two sittings on the congenital cases. 2. The outward turned sole comes into position better. 3. The simple condition of the wound when transplantation

only is performed, for experience has shown that the transplanted portion remains free from the rest of the tendo Achilles sooner if both are maintained in full extension. After the first operation the foot is in the "pointed foot" position. This is not a disadvantage, for one can then place the new Achillo-peroneal tendon shorter, and through this obtain better transplantation. In addition, one is then in a position to judge accurately just how much the end of the foot must be corrected in order to produce the best functional result. In these cases there is almost always some shortening of the affected leg, which is equalized by allowing a certain degree of the "pointed foot" portion to remain, and then compensating by a high-heeled shoe. In many cases the operation of lengthening is then not required. The author's experience with this method of treatment has been in every way most satisfactory, while operation at one sitting proved a partial failure in the two cases in which it was tried. The result was about half of what it should have been—the "pointed foot" position was there, but the anterior portion of the foot was in adduction, and the heel did not become more prominent upward and backward, as is the case in a good result.

The Use of Argyrol in the Treatment of Acute Gonorrhœa.—SWINBURNE (*Medical Record*, New York, October 11, 1902) states that argyrol comes in dark-brown scales, is very hygroscopic, and is soluble to almost any degree in water. The solutions keep well without deteriorating. It contains nearly 30 per cent. of silver. It possesses one drawback, and that is its staining properties. On account of this it has to be very carefully used, for though when treated with boiling water the stains are readily removed, yet it is distinctly disagreeable to the patient to get it on his underwear. The author has treated with this drug at a dispensary upward of 350 cases having gonococci. In the beginning the patients were given a single daily injection of 2½ to 3 drachms of a 1 per cent. solution, which was held by the patient for ten minutes in the anterior urethra. Cases in which the posterior urethra was involved received in addition a deep instillation of an ounce of the solution through a small flexible catheter, which was then withdrawn and the solution urinated out. Those cases that came regularly recovered completely in a moderately short time. After these injections there was absolutely no reaction and no pain.

In private practice the author uses several methods according to different circumstances, such as the severity of the disease, the chance of aborting the disease and the patient's ability to come frequently or not. Treatment may be daily, and in such cases irrigation with one quart of hot 1 to 1000 or 1 to 2000 solution of argyrol, followed by a 2 or 5 per cent. injection or instillation, as the case demands, with the patient's use of a 2 per cent. solution at home, once or twice a day in addition, or it may be no injections are used by the patient at home. Some patients may only be able to come once or twice a week—they get the same treatment when they come to the office, and use a 2 per cent. solution two or three times a day at home. In chronic cases good results follow the use of this drug. Cases needing sounds get now, as a lubricant on the sound, a 5 per cent. ointment, made with adeps lanæ as a base, the argyrol being rubbed up with water just enough to

render it smooth before incorporating it with the ointment. Too great stress cannot be laid on the painlessness of the drug. A 10 per cent. solution dropped in the eye hardly produces a sensation of warmth. To sum up, this drug has decided gonococcidal powers; it has a decided effect in reducing and allaying the inflammation of the disease; it can be used safely in almost any strength and at any stage of the disease; the injection can be repeated almost as frequently as the fancy of the physician dictates; the author has not seen any unpleasant symptoms due to the use of the drug and believes it to be one of the most valuable remedies given to the profession in recent years.

THERAPEUTICS.

UNDER THE CHARGE OF

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Antagonism of Morphine and Cocaine and the Employment of Cocaine in Morphine-poisoning.—DR. EDWARD T. REICHERT, in a lengthy contribution on this subject, concludes as follows: 1. That the antagonistic actions between morphine and cocaine are of a powerful and widespread character, extending to almost every function involved, and are, therefore of such a character as to justify the conclusion that one may be regarded as meeting the important indications of a successful antagonist to the other. 2. That the only important synergistic actions are as excitomotors and their tendencies in some individuals to cause syncope. 3. That cocaine is not only sufficiently powerful to successfully antagonize the profound depressant actions of morphine upon general metabolism and body temperature, but as a whole is more powerful, both relatively and absolutely, in morphinized than in normal dogs. 4. That the increase in heat production caused by cocaine is due in part to a direct excitation of general metabolic activity, chiefly by motor excitement; and that even in the absence of muscular excitement cocaine may fully counteract the morphine depression. 5. That the effects caused by a given dose of cocaine per unit of body-weight vary in intensity within wide limits. 6. That the changes in body temperature following the injection of cocaine are, with few exceptions, closely related quantitatively and qualitatively to the changes in general metabolism, and are, therefore, a fairly reliable index of the intensity of the cocaine actions —in other words, of the extent to which the cocaine is counteracting or superseding the depressant actions of morphine. 7. That the temperature coefficients in normal and morphinized dogs after cocaine are practically

identical, showing that morphine does not exert any specific actions on heat dissipation which interfere with the typical temperature-raising action of the cocaine. 8. That the typical cocaine effects may be delayed in the morphinized animal, and then appear with marked intensity, as shown by the increase of heat production, body temperature, and by motor excitation at a time when in normal animals they are lessening rapidly. Under such conditions the dangers of morphine-poisoning may be superseded by those of cocaine-poisoning. 9. That owing to a coexistent paralytic-convulsant state in the morphinized animal the administration of cocaine or other powerful excitomotor may develop or intensify the convulsant moiety, and thus render a non-lethal dose of the morphine lethal, or hasten death when the dose is lethal. In man the convulsant element is almost without exception so unimportant that there is probably little or no danger of this kind except after unnecessarily large doses of the excitomotor, or in exceptional individuals in whom the excitomotor action of the morphine is marked. 10. That the value of cocaine in morphine-poisoning probably depends chiefly upon the extent to which it antagonizes the depressant actions of morphine upon general metabolism and body temperature. 11. That the power of cocaine as a respiratory stimulant depends almost solely upon its action upon the heat mechanism. 12. That owing to the tendency of cocaine to cause syncope in certain individuals, to its excitomotor action, to the marked variability in the intensity of the effects caused by a given dose per kilo to the body-weight, to the occasional delay or latency in the typical actions of cocaine in morphinized animals, and to the fact of the greater value of small to moderate doses in morphinized dogs, it should be administered in morphine poisoning in man in small doses cautiously repeated.—*Therapeutic Gazette*, 1902, vol. xxvi., pp. 462, 518.

Camphor and the Morphine Disease.—Dr. J. Hofmann says that in healthy persons it has been demonstrated that camphor is a strong heart muscle stimulant, and that it causes an increase of blood pressure. In the initial action of morphine a directly reverse action takes place, whereas in the *habitué* stimulation is the usual result. When the morphine is withdrawn from the fiend, dilatation of the heart, with fluttering, takes place; this disappears on resuming the alkaloid. The author claims that this cardiac sensation is a vital one for the well feeling of the individual, and he believes that camphor used at such a time enables the patient to regain this sense of equilibrium. He details the history of a patient, a physician, who kept an accurate record of his sensations, for whom he recommended decreasing doses, by hypodermic injection, of morphine, and slightly increasing doses of camphor by the mouth on the advent of the patient's "abstinence" symptoms. Full tables of the progress of the case are given. Validol (a valeric acid menthol ester) was used as an adjuvant to the camphor.—*Therapeutische Monatshefte*, 1902, vol. xvi., p.360.

A Fake Morphine Cure.—Dr. O. Emmerich reports on a new cure for morphine that has appeared in the European market. Inasmuch as it has come to America, its composition as determined by the author and others should be known. It is termed "antimorphine," and is advertised as a

new remedy containing no morphine, and useful for the treatment of patients at home, "without a doctor." He found that the remedy contained large quantities of morphine, and his analysis was confirmed by the chemists of a large manufacturing house. They reported that the remedy contained 1.4 per cent. of anhydrous morphine, or the equivalent of the hydrochloride of 1.84 per cent.—*Deutsche medicinische Wochenschrift*, 1902, vol. xxviii., p. 584.

Arsenic in the Treatment of Phthisis.—Dr. H. Cybulski has been using sodium arsenate in the treatment of phthisis, with good results. He administers it hypodermically, in the following solution: Sodium arsenate, 3 grains; carbolic acid (½ per cent.), 5 drachms; 1½ minims is to be injected at one time once per diem, at body temperature. This dose is doubled every second day until 15 minims are reached. In his work, which has now extended over a number of years, as a rule twenty injections were used serially. If improvement were noted, two to three weeks were permitted to elapse and the injections renewed. The signs of improvement were increased in the body-weight and appetite, reduction of temperature, and diminution of the night-sweats. The intestinal symptoms were not affected. Diarrhœa, an uncomfortable accompaniment of arsenical medication when given by the mouth, was absent. The subjective conditions were helped. The effect of the drug on the lungs is *nil*, he thinks.—*Münchener medicinische Wochenschrift*, 1902, vol. xlix., p. 1393.

The Diphtheria Serum Question.—Professor Kassowitz returns to this subject in a second paper, in which he reiterates his former claims, and endeavors by means of charts and statistical studies to maintain his position that the diphtheria serum is of little if any service.—*Therapeutische Monatshefte*, 1902, vol. xvi., p. 499.

A Case of Poisoning from Pennyroyal.—Dr. G. W. Holland reports a case of poisoning from this drug. The patient, a married woman, aged twenty-four years, was very desirous of avoiding pregnancy, and having gone a week beyond her usual period without any appearance of the menstrual flow, applied for a prescription to "bring on the flow." Oil of pennyroyal was prescribed. At 3 o'clock in the afternoon she took seven drops, without result. The dose was repeated at 6 o'clock, with no better success. At 9 o'clock, just before retiring, she swallowed about half a teaspoonful, and soon after fell asleep. She awoke in about an hour, complaining of great dizziness and nausea. Shortly after she vomited and complained of cramps and stiffness of the extremities. She lost consciousness, and was seized with violent tonic contraction of all the muscles, opisthotonos being well marked. The spasm lasted only a few minutes, and after incoherent talking and tossing for about half an hour the toxic symptoms began to subside, and consciousness was regained. On the arrival of the physician she complained of great weakness, cramps in the stomach, and a slight desire to go to stool. The pulse was 108 and feeble. Respiration and pupils were normal, and as the toxic symptoms were subsiding the author gave nothing, and merely watched the course of the symptoms. The following morning the patient

was able to attend to her regular duties. The desired effect of bringing on the flow was not accomplished. The toxic dose in this case was half a drachm, and from the symptoms which were produced it is evident that the drug should be administered with great caution.—*Virginia Medical Semi-Monthly*, 1902, vol. vii., p. 319.

Treatment of Typhoid Fever.—Dr. Francois Bouchard gives the results of a detailed study of intestinal antisepsis in the treatment of typhoid fever after the method of Teissier. In 1890 this author described his method as follows: (1) Morning and evening a capsule of naphthol, 7 grains, and 4 grains of bismuth salicylate; (2) four cold enemata a day, to encourage diuresis; (3) following the afternoon enema, an enema of 1 drachm of extract of cinchona and 15 grains of quinine sulphate, dissolved in an infusion of valerian; this is used as antithermic and tonic; (4) the diet is liquid—a little milk, ten ounces of white wine, broths, etc. As a result of this method in 151 patients treated during twelve years the statistics showed a mortality of 4.63 per 100. He believes that the temperature, the abdominal and digestive symptoms, and the general condition are all much improved. Convalescence is shorter, and complications, particularly the intestinal complications, are much rarer. The effects of the treatment commence to show only on the fourth day.—*Thèse de Lyon*, 1902, No. 177.

Impermeability of the Lung for Ammonia.—Dr. R. Magnus determined to test the permeability of the lung for this gas. By intravenous injection minute doses of ammonia cause the most intense irritation of respiration, convulsions, and disturbances of circulation and of the central nervous system. The statement of Knoll that in tracheotomized and vagotomized animals the long-continued inhalation of ammonia is harmless, seems, in the light of these facts, so astonishing that the following test was made: Tracheotomy was performed on a rabbit after the vagi had been cut, and the animal allowed to inhale air saturated with ammonia. No constitutional symptoms, only local irritation of the mucous membranes followed, while if sulphuretted hydrogen was substituted for the ammonia, death occurred in fifteen seconds. The experiment was then modified so that ammonia was injected into the veins and the expired air passed into Nessler's reagent, yet in no instance was a precipitate obtained, despite the fact that the blood, on autopsy, had a bright-red color and smelt strongly of ammonia. The experiment was then repeated by injecting directly into the pulmonary artery, with the same result. If, however, artificial respiration were kept up after death, the reagent soon became cloudy. The experiments showed that the impermeability is a property of the living tissues.—*Archiv für Experimental Pathologie und Pharmakologie*, 1902, Band xlviii., p. 100.

Affinity of Carbonic Oxide for Hæmoglobin.—Dr. G. Huffner says that if hæmoglobin is exposed to a mixture of carbonic oxide and oxygen it will combine with both gases; but since the affinity of the substance for carbonic oxide is much greater than for oxygen, even small amounts of the former present in the atmosphere will render a large percentage of the blood unfit for oxygenation. He has constructed a table of percentages,

from which it is evident that with but 0.05 per cent. of carbonic oxide in the air as much as 27 per cent. of the hæmoglobin present is seized upon by the poisonous gas.—*Archiv für Experimental Pathologie und Pharmakologie*, 1902, Band xlviii., p. 87.

GYNECOLOGY.

UNDER THE CHARGE OF

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Laparotomy for Adherent Retroflexion during Pregnancy.—DOLERIS (*La Gynécologie*, June, 1902) treats this condition by opening the abdomen, separating adhesions, and shortening the round ligaments. He reports a successful case in which the patient, who was in the third month of pregnancy at the time of the operation, was delivered easily at full term, the uterus remaining in its normal position after involution had occurred.

Lymphangiectasis of the Vulva.—DURET (*Journal des Sciences Méd. de Lille*, 1902, No. 5) believes that there is a form of this disease which is due to streptococcus infection as well as to filaria. The superficial variety affects principally the external genitals and lower limbs, and is usually accompanied by œdema and elephantiasis of the skin; small vesicles appear, which may open spontaneously, causing a copious discharge of lymph, which may be so profuse as to lead to profound anæmia, which, however, yields to constitutional treatment.

Premature Menopause.—ADDINSELL (*British Medical Journal*, May 17, 1902) reports the case of a young woman, aged twenty-six years, whose menstruation had been entirely normal up to the time of her marriage. During the wedding journey she was under great excitement at the time when her monthly flow was due. It had never appeared since. When examined six years later she was in good health, although she suffered from flushes of heat, which occurred every few weeks. Her uterus had undergone senile atrophy, the sound entering to the depth of an inch. The ovaries were apparently normal. The patient stated that her sexual desires were preserved, and that her breasts sometimes became swollen and tender.

Structure of the Senile Uterus.—VERRONI (*Annali di Ostetricia et di Ginecologia*, 1901, No. 7) presents the results of his studies of twenty-eight normal uteri removed from women between the ages of sixty and ninety-two. In most of the specimens the mucous and submucous layers had undergone atrophy, together with the glands; in others, the submucous layer was

thickened and the glands were actually hypertrophied. The capillaries were numerous and tortuous, and many groups of leucocytes and infarcts were observed. In general, the epithelium of the cervical canal was well preserved and the glands cystic.

The smooth muscular fibres were present, without marked degeneration, but with an excess of fibrous tissue. Vacuoles, infarcts, and collections of leucocytes were scattered throughout the muscular layer. The bloodvessels were intact, the capillaries being often visible to the naked eye. While the endothelium of the larger vessels presented a normal appearance, there was marked hypertrophy of the tunica, with frequent calcareous degeneration. The writer believes that the anatomy of senile uteri proves that the condition is the result of normal involution, and not of an inflammatory process.

Sterilization of Phthisical Women.—NEUMANN (*Centralblatt für Gynäkologie*, 1902, No. 12) criticises Pincus' plan of abolishing the risk of pregnancy in phthisical subjects by destroying the endometrium by atmokausis. The writer prefers resection of the tubes for several reasons, psychical and physiological, as menstruation is preserved and the patients are spared the mental and physical disturbances of the menopause. His operation, which is safe and easy, consists in excising a wedge from each tube and suturing the ends without disturbing the ovaries.

Intra-abdominal Pressure.—KOSSMANN (*Centralblatt für Gynäkologie*, 1902, No. 27) replies to a former article of Meyer, who denies the existence of a true intra-abdominal pressure. While agreeing with the latter in his assertion that this pressure is constantly changing and that it is never negative, he denies that it varies at every point in the cavity. The writer claims that this pressure is everywhere alike, and is only unequal when gas or fluid is abnormally present in the free cavity. Intra-abdominal pressure becomes a disturbing factor, he believes, when it is sufficient to overcome the normal power of resistance of the muscular wall.

Perforation of the Uterus.—SCHULZE-VELLINGHAUSEN (*Centralblatt für Gynäkologie*, 1902, No. 27) reports two cases of accidental perforation of the non-pregnant uterus with the sound, in both of which the organ was subsequently extirpated and was carefully examined microscopically. The writer concludes that not only do atrophy, tuberculosis and malignant disease of the uterus favor accidental perforation of the non-puerperal uterus, but also degenerative changes in the muscular wall. The accident is by no means uncommon, and great care should be observed in deciding these cases medico-legally, especially when the question of undue violence or want of skill is brought up.

[The question naturally suggests itself: Why was it necessary to remove the uterus in the two cases reported? The accident is seldom followed by any serious results under aseptic conditions.—ED.]

The Paravaginal Incision in Hysterectomy.—SCHAUTA (*Monatsschrift fur Geb. u. Gyn.*, Band xv., Heft 2) is not enthusiastic over the radical

abdominal operation for cancer of the uterus, since in two of his patients who succumbed to the operation neither the glands which were extirpated nor those which remained were diseased. It has not yet been satisfactorily demonstrated that cases in which cancerous glands have been removed remain free from recurrence. Any comparison between the conditions in the pelvis and axilla is unjustifiable. Most stress should be placed upon the removal of the cancerous foci that are nearest to the uterus, and this is accomplished by Schuchardt's paravaginal method, which the writer has practised in thirty cases, with five operative deaths. Some of these were inoperable by other methods; in fact, his proportion of operable cases has risen from 15 to 46.5 per cent. In the cases reported the bladder was wounded four times, the uterus three, and the rectum once. If the pelvic lymph glands are affected the operation is to be regarded as simply palliative.

[No comment is necessary, except to call attention to the writer's own statistics and his admission with regard to the cases selected for operation. —Ed.]

Tuberculosis of the Appendix and Adnexa.—Kraus (*Centralblatt für Gynäkologie*, 1902, No. 27) reports a case in which a nullipara, aged thirty years, gave a history of appendicitis ten years previously. A tumor was discovered in Douglas' cul-de-sac, which, at the operation, proved to be an enlarged ovary and a tubercular tube and appendix. An interesting point was the fact that the tubercles were confined to the mucous membrane of the distal end of the tube and to the adherent tip of the appendix. The reporter concludes that the process began in the appendix and extended outward to the Fallopian tube, possibly along the appendiculo-ovarian ligament. The ovary was the seat of an abscess, but no tubercles could be found, nor were tubercle-bacilli observed in any of the sections.

The Malignancy of Solid Embryomata.—Jung (*Centralblatt für Gynäkologie*, 1902, No. 15) affirms that solid and cystic embryomata present no essential points of difference. The former, as well as the latter, are to be regarded as benign in character and are parasites rather than true neoplasms.

He reports two cases. In the first the cystic element predominated. The solid portion contained not only the usual epidermal structures, but nerve tissue, cartilage, bones, and numerous pouches lined with columnar epithelium and surrounded by smooth muscle fibres. The peritoneum and omentum were studded with grayish nodules, and the retro-peritoneal glands were enlarged as high up as the transverse colon, but no trace of sarcomatous degeneration was found microscopically. The nodules proved to be not metastases, but simply obliterated vessels. The patient was in good health a year and a half after the operation and had gained twenty pounds.

In the second tumor all three embryonic layers were represented, the connective tissue being so rich in cells that malignancy was suspected; but the subsequent history of the patient proved the contrary.

The writer calls attention to the fact that twelve of the twenty cases of teratoma recorded are described as being either undoubted sarcoma or sarcomatous in appearance. Cancerous degeneration of these growths has not

hitherto been described, though he thinks that it might occur. Only one genuine case of retroperitoneal metastasis of a teratoma has been reported by Ewald, which is a strong argument against its malignant character. The prognosis is accordingly good, and the tumor should always be removed.

Abscess of the Uterus.—Franqué (*Sammlung klin. Vorträge*, No. 316) bases his paper on this subject on twenty-eight doubtful and fifteen clear cases collected from the literature. The condition is due to puerperal sepsis, and may terminate by perforation of the uterus and general peritonitis, or the patient may recover, with atrophy and obliteration of the organ. Repeated chills and elevation of temperature, associated with prolonged discharges of pus, enlarged and tender uterus, should point to the probable condition. The diagnosis is difficult, however, since a suppurating sarcoma or fibromyoma may be easily mistaken for it, even when it follows labor. The prognosis is most unfavorable, the mortality without operation being 75 per cent. Incision and drainage of the abscess through the cervical canal is dangerous; it is advisable only when the abscess has ruptured into the uterine cavity. In chronic cases vaginal extirpation of the uterus may be performed, but the abdominal route is preferable. If the abscess is small and localized and the adnexa are healthy, it may be possible to attach the uterus to the abdominal wound, incise, and drain, but abdominal hysterectomy will usually be necessary.

Menopause.—Kleinwachter (*Centralblatt für Gynäkologie*, 1902, No. 20) presents some personal observations based on 373 cases. Assuming that the normal menopause occurs between the ages of forty-five and fifty years, he found that in 130 women the climacteric atrophy of the internal genitals was present too early. In 40 menstruation did not cease until after fifty years; 13 were fertile at 45 years and over. Senile endometritis was noted in 7 cases. In 4 women between the ages of fifty-eight and seventy-one years, who had always enjoyed good health since the menopause, metrorrhagia appeared, due, the writer inferred, to calcification of the uterine vessels since no other cause could be assigned.

Artificial Distention of the Bladder.—Desguin (*Journ. de Chir. et Ann. de la Soc. Belge de Chir.; Centralblatt für Gynäkologie*, 1902, No. 23) recommends that in cases of prolapsus the bladder should be distended to its utmost capacity before beginning an anterior colporrhaphy or vaginal hysterectomy, in order that the organ may be lifted out of the pelvis. He injects from two to two and one-half pints of boric acid solution.

Fibromyoma of the Urethra.—Lörmberg (*Upsala Läkereförenings Förhandlingar; Centralblatt fur Gynäkologie*, 1902, No. 34) has collected twenty-seven cases from the literature, to which he adds the following: The patient, aged thirty-one years, was admitted to the hospital on account of hemorrhage from the urethra without other symptoms. On examination a tumor the size of a hazelnut was seen in the dilated urethral opening; it was eroded, quite sensitive, and bled easily. The growth was easily shelled out of its capsule.

OBSTETRICS.

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Pubiotomy.—At a meeting of the Netherland Gynecological Society, VAN DE VELD (*Centralblatt für Gynäkologie*, 1902, No. 4) reported the case of a woman, aged twenty-eight years, in her second labor. Her first child was premature and perished soon after birth. The patient had been in labor twenty-four hours and had a rapid, feeble pulse, while the contraction ring in the uterus was plainly formed and the head had not yet entered the pelvis. The internal antero-posterior diameter was 8½ cm. The heart sounds were good.

On account of the presence of the contraction ring, version was declined. Because the child was living, craniotomy was also declined, while Cæsarean section was not attempted because the pulse of the mother was high and the amniotic liquid was foul. The operator chose pubiotomy, because the wound through the ramus of the pubes would be less easily infected than the open pubic joint. The operation proceeded successfully, and a living child was born. On the third day the mother had a mild attack of thrombosis on the left side where the incision was made. On the eighteenth day the patient was convalescent.

Rupture of the Uterus Through Cicatricial Tissue.—In the *Centralblatt für Gynäkologie*, 1902, No. 4, PEHAM reports the case of a patient in her fourth pregnancy who had a justo-minor pelvis. Her history showed that the first confinement proceeded naturally, and that in the second labor the patient was brought to the hospital with complete rupture of the uterus. The intestine prolapsed through the uterine tear. The laceration began 1 cm. above the anterior lip of the cervix and extended considerably toward the right side and above. The intestine was replaced by the insertion of the hand into the uterus, iodoform gauze was carried through the rent into the abdominal cavity, and the lower uterine segment and vagina were packed with sterile gauze. The patient made a good recovery and was discharged, about three weeks after her admission, in good condition. Two years later the patient again became pregnant and had an abortion at about seven months. She recovered without accident.

She was again admitted to the hospital in active labor near full term. She complained that a few hours previous she had experienced a sudden and severe pain as if something in the abdomen had suddenly torn. Labor pains stopped, and a physician who was summoned sent her to the hospital.

Upon examination her temperature was slightly subnormal, her pulse 90,

and she gave little evidence of rupture of the uterus. The uterine muscle was not firmly contracted, there was no hemorrhage, the head of the child was movable above the pelvis, and no heart sounds or fœtal movements could be obtained. On vaginal examination a laceration was found on the right side, the upper end of which could not be reached from below. The cervix admitted three fingers without difficulty, the membranes had ruptured, and the head was movable above the pelvic brim. There was a discharge of dark-colored blood from the genital organs. The pelvis was considerably contracted, and delivery was accomplished by craniotomy. This was followed by no hemorrhage, but by a considerable failure in the pulse. On vaginal examination a rupture of the uterus was easily found, and through the rupture the umbilical cord led to the placenta, which had escaped into the abdominal cavity. The abdomen was opened as soon as possible, and the placenta found slightly adherent to a portion of the omentum. Hysterectomy was immediately performed, with the removal of the uterine appendages. The patient made an uninterrupted recovery. On examining the uterus its contractile portion was found very strongly developed, but the remainder of the womb was deficient in strength and elasticity.

A second and similar case also reported is that of a patient in her second labor who had a flat rachitic pelvis. The patient was admitted to the hospital with normal pulse and temperature, the child well developed and the head above the brim of the pelvis. The membranes were unruptured, but labor had not proceeded. After the patient had been under observation for some time, and it was seen that she could not deliver herself, version was performed under anæsthesia, and the child was extracted. It was somewhat asphyxiated, but revived. The placenta was spontaneously expelled, and the uterus contracted well. An abnormal bleeding continued from the womb, and, upon examination, rupture of the uterus was found extending through the right side of the lower uterine segment to the peritoneal tissue above.

The treatment consisted of irrigation of the womb with lysol, and packing with iodoform gauze. Cold applications were placed over the abdomen, and tincture of opium was given. The patient made a good recovery.

When the history of her first labor was obtained it was found that version had been performed, followed by an unusually difficult extraction, and that a laceration had then occurred through the same tissues, following the version and extraction.

The third case was a patient in her third labor with contracted pelvis, at whose first confinement three years previously it was necessary to incise the cervix to perform craniotomy. At her next labor she was delivered of a child by breech presentation, and had fever during her convalescence.

In her present illness she had received a severe injury by straining and falling, and considerable amniotic liquid had escaped. This happened four days before admission, and the patient had a chill the night previous. On admission she was greatly weakened, and on examination the fœtus was found in transverse position. Upon vaginal examination the scar was found upon the right side of the cervix, extending through the entire cervix and somewhat above. Similar scars were also present in other portions of the cervix. The membranes had ruptured and the thigh of the child could

be felt within the uterus. The heart sounds were loud and strong, and as dilatation proceeded the right arm could be detected. The cervix was incised and version was performed with extraction, the scars being incised as the extraction proceeded to avoid serious injury. The extraction of the arms was so difficult that the child died during this manipulation, and craniotomy was performed upon the aftercoming head. Upon examination a tear was found through the lower uterine segment upon the right side, extending to the peritoneum. The patient was treated by gauze packing as in the other cases and made a tedious recovery. Her illness was complicated by facial erysipelas and by parametritis upon the right side of the pelvis.

[The writer gives no reason for choosing the method of delivery employed in preference to that by abdominal incision. It seems to us that a considerably contracted pelvis, with the history of rupture of the uterus in former labor and with the presence in two of the cases of a living child, justified delivery by abdominal incision. The selection of version in a case where rupture of the uterus had formerly occurred seems inexplicable.]

Vaginal Use of Elastic Bags.—Voigt (*Archiv für Gynäkologie*, 1902, Band lxvi., Heft 1) reports from the clinic in Dresden the vaginal use of elastic bags during labor in 510 cases among 12,445 labors. This was practised under antiseptic precautions, the bags being carefully cleaned by soap and water, by bichloride of mercury, and the vagina douched with bichloride of mercury before the bag was inserted. Three indications were recognized as justifying this practice: The necessity for retaining the amniotic liquid when premature rupture of the membranes occurs or is threatened, the dilatation of the soft parts, and the stimulation of uterine contractions. The last indication is regarded as questionable, and Voigt believes that ordinarily elastic bags should not be used for this purpose.

In cases of contracted pelvis spontaneous labor seemed to be stimulated by this procedure, although pelvic contraction is not a valid indication for the use of the bag. In cases where the pelvis is slightly flattened where version is determined upon, and where the operator wishes to retain the amniotic liquid as long as possible, this method has decided advantage. In a highly-contracted pelvis, through which a child cannot be delivered alive, it would not only do no good, but positive harm.

In cases of deep attachment of the placenta and placenta prævia this method is inferior to the use of the tampon of antiseptic gauze. In eclampsia where labor is advanced sufficiently to make delivery possible in a short time these bags were of use in dilating the soft parts for labor.

In some cases where labor must be hastened in the interests of the child this method was of use, as it increased the uterine contractions and dilated the vagina and pelvic floor. In some cases it was seen to be useless, as cicatricial contraction or rigidity was so great as to prevent the good result from the method.

The pains must have already begun to make this method of value, and there must be no cicatricial contraction of the cervix, which must be dilated to admit one or two fingers; the bag should be moderately filled only when it gives but little discomfort to patients and does not prevent sleep between the pains. Its use does not influence the puerperal period unfavorably, but

hastens convalescence by preventing exhaustion. In the interests of the child it shortens labor, and thus lessens the danger of fœtal death.

Urobilinuria during Pregnancy as a Sign of Fœtal Death.—In the *Annali di Ostetricia*, 1902, No. 4, MERLETTI reports a series of investigations to determine the presence of urobilinuria in pregnancy and to what extent it increases at the death of the fœtus. He found that it exists in most cases of pregnancy, and that it gradually but considerably increases in the event of fœtal death.

Quintuplets.—In the *Sei-I-Kwai Medical Journal*, 1902, No. 3, vol. xxi., SATO reports a case of multiple birth with five fœtuses.

The mother was a multipara, aged thirty-seven years. She married at fifteen years, and had borne a number of children, with easy parturition. There was an heredity of multiple conception on the side of her father's family. The last menstruation appeared in April, and parturition took place at about the eighth month of pregnancy. Her physicians were not summoned until she was in active labor, when it was learned that she had experienced considerable inconvenience during pregnancy through excessive size and general dropsy, well marked in the lower extremities. She worked as usual until a few days before parturition. She had supernumerary nipples. Labor proceeded spontaneously. The first child, a boy, was delivered, covered with the membranes; four minutes afterward the second child, a girl, was delivered; five minutes later the third child, a boy, was born, followed by a common placenta for the first and second children; after another five minutes the fourth child, a girl, was delivered by the feet, and another placenta for the third and fourth children was expelled. It was then supposed that all of the children had been delivered.

On examining the abdomen a fœtal head was felt above the navel, and upon gentle pressure the fifth child, a boy, was brought down and delivered. A single placenta for the fifth child was shortly afterward discharged. There was a moderate hemorrhage, which ceased upon tamponing and compressing the uterus.

The first placenta weighed 666 grammes, the second 685 grammes, and the third 277 grammes. The weight of the children varied from 1111 grammes to 1555 grammes. The children were inferior in development, and soon succumbed.

The Estimation of the Transverse Diameter of the Pelvis in the Parturient Woman.—SANDSTEIN (*Journal of Obstetrics of the British Empire*, October, 1902) contributes a paper in which he gives the results of his measurements of the pelvis to obtain the transverse diameter in the parturient woman. After a thorough study of various sorts of pelves he comes to the conclusion that for practical purposes the transverse diameter of the pelvic brim is to be estimated in any pelvis by simply dividing the intercristal diameter by two. This very simple method will enable the obstetrician, from external measurements, to deduce the important measurements desired internally.

DISEASES OF THE LARYNX AND CONTIGUOUS STRUCTURES.

UNDER THE CHARGE OF

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Rapid Development of a Fibrosarcoma of the Tonsil.—At a meeting of the Chicago Laryngological and Climatological Association, April 21, 1902 (*Journal of the American Medical Association*, May 24, 1902), Dr. Charles M. Robertson narrated the case of a farmer, aged sixty-two years, who acquired an extensive fibrosarcoma of the tonsil and soft palate, which began in a small swelling above the left tonsil a few days after that organ had been pricked with a straw in use for picking the teeth. By the end of eight weeks it had developed into a large tumor occupying the left palatal arch, well down to its base, involving the tonsil and the side of the pharynx as far as the epiglottis, and up behind the edge of the hard palate as far as the left Eustachian tube. It extended forward into the mouth to within one inch of the incisor teeth. The following week the growth was removed under chloroform anæsthesia, and was found to be encapsulated. Twenty months had passed without recurrence.

Œdematous Laryngitis.—Dr. F. E. Ross, of Erie, Pa., reports the following case (*American Medicine*, May 24, 1902) in an habitual drunkard, aged forty-three years, complaining in great distress of inability to talk or swallow, found to be due to an œdematous uvula as large as a man's thumb, and which was relieved by scarification. Three hours later Dr. Ross was summoned to a saloon, where he found the same man suffering with intense dyspnœa, for which he opened the trachea with a tenotome from his pocket case, and kept the wound patulous with a pair of uterine forceps. The patient was taken to a hospital and a tracheal tube inserted. Although the dyspnœa was relieved, the œdema progressed so that by the evening of the first day the whole anterior and lateral cervical regions were enormously distended, the effusion extending down over the clavicles on to the chest. At the end of the first day it began to subside, and on the third day the tube could be removed. The patient left the hospital upon the eleventh day. As to etiology, the œdema was believed to be of nephritic origin.

Adenoma of the Nose, with Incipient Sarcomatous Metamorphosis: Removal by External Access.—Dr. Emil Mayer, of New York, reports (*American Medicine*, August 2, 1902) a case of an Irishman, aged sixty-eight years, who had suffered for twenty years, subsequent to a kick from a horse, depressing his nose and producing obstruction to his breathing. During the six years previous to his being sent to Dr. Mayer his physician had removed numbers of polypi, with some relief; but during the last year the character of the growth had so changed that he suspected sarcoma and advised radical

procedure. Dr. Mayer found the left side of the nose deformed, with a large tumor on the left occluding both nasal passages. The entire hard palate was depressed and the presenting tumor soft and yielding, the growth extending into the posterior nares, and the slightest touch produced hemorrhage.

The nose was cut through on the left and drawn aside with retractors, revealing an immense growth, which was thoroughly evulsed with forceps and curette. "It was found that the whole mass had originated from the left middle turbinated bone, and this place was thoroughly cauterized. There was entire absence of the vomer, the nasal bones on the left, and of most of the superior maxilla that formed the hard palate. The cartilaginous septum was not affected, while the bones had become entirely absorbed. There was no evidence, however, of involvement of the bone so far as the growth was concerned; hence no part of the superior maxilla was removed. The patient made an excellent recovery." The examination of the tumor showed it to be formed mainly of papilliform adenomatous tissue, the balance consisting of small myxomatous polypi.

Phlegmonous Laryngitis —At the meeting of the Chicago Laryngological and Climatological Association, April 21, 1902 (*Journal of the American Medical Association*, May 24, 1902), Dr. O. T. Freer read the history of a "Case of Phlegmonous Laryngitis Terminating in Abscess in Front of the Larynx," in a man, aged fifty-four years, who had never been ill before. It suddenly began in the night in a glossitis, attendant with dyspnœa and tumefaction around the larynx, with gradually increasing stenosis, which necessitated tracheotomy on the tenth day, and it was forty days before the canula could be dispensed with.

Supernumerary Uvula.—Dr. Joseph Mullen, of Houston, Texas, depicts (*Laryngoscope*, May, 1902) a case of this anomaly in a male negro, twenty-five years of age, well developed and in apparent good health.

Fatal Membranous Glossitis.—At the meeting of the Toronto Clinical Society, May 7, 1902 (*Journal of the American Medical Association*, May 24, 1902), Dr. A. J. Harrington reported an unusual case of membranous glossitis, of which he stated he could find no trace in the literature. The specimen was presented. The condition occurred in an infant, aged eleven months—a fine, healthy, robust child. It had measles in March, 1902. On April 8th the whole cast of the tongue exfoliated, and the system of the child was thoroughly saturated with sepsis. The child died the following morning.

A Durham Tube in the Right Bronchus.—Dr. E. D. Ferguson, of Troy, reports (*American Medicine*, February 1, 1902) a case in which the outer canula of a Durham tracheotomy tube had fallen into the right bronchus, owing to lack of the collar at the distal extremity in front of the shield. After an extensive incision of the trachea, nearly to the bifurcation, the missing canula could be felt by the finger in the right bronchus, and its upper edge was seen by reflected light from a head mirror, so that it was

promptly removed with forceps. The patient, a woman, aged forty-two years, made an excellent recovery.

The Chemical Pathology of the Saliva and of the Pharyngeal Secretions as a Means of Diagnosis.—A paper on this subject was read by Dr. D. Braden Kyle, of Philadelphia, before the Twenty-fourth Annual Congress of the American Laryngological Association (*American Medicine*, July 12, 1902). Examination of the salivary reaction by the use of litmus paper in the mouth is practised more or less frequently in attending to buccal, oral, and pharyngeal diseases, but special chemical investigation of the constituents of the secretions is rarely practised. In the paper before us the writer refers to his own observations commencing in 1895–96, and also to those of the dentists Michaels, of Paris, and Kirk, of Philadelphia; and he believes that a good many throat and nasal affections, reflex and otherwise, could probably be traced in origin to perverted salivary secretion.

DERMATOLOGY.

UNDER THE CHARGE OF

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The Occurrence of Bullæ in Lichen Planus.—Whitfield (*British Journal of Dermatology*, May, 1902) reports the case of a single woman, twenty-seven years old, in whom an extensive eruption of lichen planus was accompanied by vesicles and bullæ upon the legs and feet. A histological examination of the fluid found in the bullæ showed a small number of leucocytes, of which about 20 per cent. were eosinophile and the remainder polynuclear. There were also a few staphylococci and streptococci present. As to the relation of arsenical treatment to the occurrence of this unusual complication, the author found that out of seventeen reported cases nine had not taken arsenic before the appearance of the bullæ. In most cases the bullæ corresponded exactly with the papular lesions. No constant blood alteration, such as eosinophilia, etc., was present.

A Case of Hyphomycetic Granuloma of the Skin.—Schamberg (*Journal of Cutaneous and Genito-Urinary Diseases*, September, 1902) reports the following interesting and unusual case: A woman, aged forty years, had upon the right forearm two large patches elevated a half-centimetre or more above the surrounding skin, having a mammillated surface almost papillomatous in character; they were of a dull red color, firm to the touch, and quite tender.

A few days after coming under observation a pustule developed a short distance from one of the patches, which rapidly increased in size, ruptured, and became a small, rapidly growing tumor of granulation tissue. From time to time other pustules appeared which followed the same course. Under applications of acetanilid and a weak solution of permanganate of potash marked improvement took place. Microscopic examination of sections showed a fungus consisting of mycelial threads staining with gentian violet scattered throughout the cell-infiltration in the corium. Culture and inoculation experiments were negative. As the author was not certain of the trichophytic nature of the fungus he preferred to report the case as a hyphomycetic granuloma.

Primary Actinomycosis of the Occiput.—BOHM (*Archiv für Dermatologie und Syphilis*, Bd. lix., Heft 3) reports a case of primary actinomycosis occurring in the occipital region. The patient, a butcher, twenty-six years old, had an acute inflammatory swelling, accompanied by fever and pain. Under treatment with ice-bags and solution of acetate of lead the inflammatory symptoms subsided, but the swelling remained. After a time scattered, firm nodules appeared in the swollen parts, which slowly underwent softening, forming abscesses which opened spontaneously. In the fluid evacuated from these abscesses were yellowish-gray granules, which were found by microscopic examination to contain the actinomyces fungus. After dividing the fistulæ, pure tincture of iodine was injected, which produced marked improvement, so that after two months' treatment, during which about twenty-five injections were made, the disease was cured. No recurrences have taken place in three years. The author thinks infection occurred through scratching the scalp with the fingers, which had been soiled by handling the flesh of an actinomycotic bullock or hog.

Psoriasis following Nervous Shock.—BALZER and FAURE-BEAULIEU (*Annales de Dermatologie et de Syphiligraphie*, 1902, No. 6) at a recent meeting of the Sociètè Française de Dermatologie et de Syphiligraphe reported the case of a man, aged fifty-four years, who, after seeing one of his children narrowly escape being run over by a tram-car, was seized with nervous trembling, chills, and fever so severe as to confine him to bed. The next day red spots were noticed upon the left forearm which were followed in a day or two by others upon the chest and legs. Fifteen days later, upon his admission to the hospital, he presented a typical guttate psoriasis. The patient had never had any cutaneous affection previous to this attack of psoriasis, nor was psoriasis present in any member of his family.

A Case of Dermatitis Verrucosa Probably Caused by the Bacillus Coli Communis.—ANTHONY (*Journal of Cutaneous and Genito-Urinary Diseases*, August, 1902), under the above title reports a case in which a lesion clinically resembling tuberculosis verrucosa cutis followed a burn with muriatic acid. At the base of the thumb was a patch of vegetating papillæ surrounded by a red zone one centimetre wide, in which were numerous small abscesses from which a drop of pus could be evacuated by pressure; pus could also be squeezed from the apices of many of the papillæ. Blastomycosis, tubercu-

losis verrucosa cutis, and streptococcic dermatitis were excluded. With ordinary stains a short bacillus was found in the pus which was fully identified as the colon bacillus. Examination of sections showed an enormous proliferation of the epithelium of the epidermis. Here and there were formations resembling, in a slight degree, the so-called epithelial pearls found in cancer of the skin, but these were not at all typical. Small abscesses were also present which were filled with polynuclear leucocytes.

The Treatment of Lupus Vulgaris by Applications of Radium.—HALLOPEAU and GADAUD (*Annales de Dermatologie et de Syphiligraphie*, 1902, No. 71), at a séance of the Société Française de Dermatologie et de Syphiligraphie, presented a patient with a verrucose lupus vulgaris of the hand which had been much improved by applications of radium. The first application was made during seventy-two hours, and produced a lasting discoloration; fifteen days later ulceration followed. Two months later another application of radium was made, lasting one hundred and twenty hours; this produced a loss of substance which still persisted. Seven other applications were made of twenty-four hours' duration; these left no trace. Compared with the condition presented during former visits to the hospital, the improvement was very considerable. The verrucous elevations had disappeared, leaving a smooth cicatrix of healthy aspect.

Upon the same occasion (*Ibid.*) Danlos reported four cases treated in the same manner, and expressed the opinion that there was a great future for radium in dermatotherapy. Its employment was justifiable in erythematous lupus and lupus vulgaris, in hypertrichosis, superficial cancers, nævi, etc.

Psoriasis following Vaccination.—DORE (*British Journal of Dermatology*, September, 1902), at a meeting of the London Dermatological Society, presented three patients in whom a more or less extensive psoriasis appeared after vaccination. The first patient was a young man, aged twenty years, without any history of a previous skin affection. On the eighth day after a revaccination a red, scaly eruption appeared upon the legs, which soon extended to the arms and trunk. Upon appearing at the hospital he presented an extensive psoriasis, which differed from an ordinary attack only in the fact that the site of the vaccination was marked by circular, red, scaly patches. The second case occurred in a woman, aged thirty years. The vaccination did not heal for two months, and eventually became covered with red, scaly patches, which were followed by others on various parts of the body. When seen she had typical psoriasis. The patient was otherwise healthy, and had not had any skin affection previously. The third case was a young woman, aged eighteen years, in whom, after vaccination, a "red, patchy rash" appeared which, disappearing in three days, was followed by psoriasis presenting the usual features. In this case there was a history of an eruption at eleven years of age resembling the present one.

Noma and Hospital Gangrene.—MATZENAUER (*Archiv fur Dermatologie und Syphilis*, Band lx. Heft 3) in a recent paper attempts to prove that, clinically as well as bacteriologically, noma and hospital gangrene are identical processes. From a study of the literature of the affection it is evident that

noma occasionally occurs epidemically; and the circumstance that numbers of cases quickly follow one another in institutions proves that it is transferred from one patient to another. It always develops where there are already defects in the mucous membrane. Clinically there is no definite dividing line between noma and hospital gangrene; they are both an inflammatory process which early leads to coagulation necrosis of the tissues. The bacilli found in noma agree in form, size, and tinctorial characteristics with those in hospital gangrene. The author concludes that, since clinically no definite line can be drawn between these two affections, and since the histological and bacteriological findings are the same, noma can only be regarded as a form of hospital gangrene.

An Anomalous Superficial Dermatitis Occurring during Typhoid Fever and Having Some Resemblance to Psoriasis Rupioides.—ROLLESTON and MERCER (*British Journal of Dermatology*, June, 1902) report the case of a married woman, aged twenty-eight years, with a typical attack of pronounced typhoid fever, in whom, besides the ordinary typhoid roseola upon the abdomen, there was an eruption of peculiar round and oval lesions resembling the early stage of seborrhœic eczema. These rapidly increased in size and number, there being about twenty small round circles and oval areas of varying sizes. The lesions began as erythematous macules, slightly rough to the touch, and scarcely raised above the surface. A greasy, brownish-gray or greenish scale formed on this erythematous base resembling closely a flat limpet in shape. Upon the flattened apices of several of these scales there were yellowish, cheesy nodules, but no distinct pustulation. The scales after a time separated spontaneously, the skin beneath being normal in the centre, but presenting an erythematous margin which gradually broadened and faded, in this way producing confluent rings. The eruption was practically limited to the lower part of the chest and front of the abdomen. Bacteriological examination showed the staphylococcus albus, but no typhoid bacilli nor any fungus.

OPHTHALMOLOGY.

UNDER THE CHARGE OF

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Etiology of High Myopia.—GUTTMANN, Breslau (Graefe's *Archiv. of Oph.*, 54, ii.), analyzes ten years' clinical material in Professor Magnus' polyclinic. Of 49,200 patients—48.9 per cent. males, 51.1 per cent. females—3688 were affected with myopia of both eyes (anisometropia excluded),

equalling 7.5 per cent., a proportion not greatly different from that of other Continental clinics. Of these, 57 per cent. occurred in males and 43 per cent. in females, confirming previous statistics as to the greater liability of the male sex to myopia.

Of high degrees, 6 D. and upward, there were in round numbers 1000—27 per cent. of the total number of myopes and 2.1 per cent. of the entire clinical material. A striking result comes out from the study of these 1000 cases as regards the proportion of the sexes affected with high myopia, viz., 36 per cent. in males and 64 per cent. in females, almost the direct opposite of the proportional distribution of low myopia. It appears that high myopia is about twice as prevalent in the female as in the male sex. This striking excess admits of but one explanation, viz., that such myopias, not dependent upon close work, are largely cases of essential myopia, to which the female sex shows a special predisposition.

From a further analysis the author concludes that three-fourths of all cases of myopia of high degrees are instances of essential myopia, and but one-fourth is found in subjects who have been engaged from an early age at very close work—occupational myopia. The latter form is about equally prevalent in both sexes, whereas the female sex is more than twice as liable to essential myopia. Of high myopias in men one-third are dependent upon close work, and but one-fifth in women. Occupational myopia of 10 D. and over is much rarer than essential myopia equally high. Complications of the fundus occur in 28 per cent. of high myopia. Accordingly the female sex is more than twice as predisposed as the male. Of the complications the most frequent is lesion of the macula. Detachment of the retina is rare. High essential myopia is more likely to be attended with complications than similar degrees of occupational myopia.

In over two-thirds of all instances of high myopia, essential and occupational, no hereditary influence can be traced.

A Study of the Sense of Sight Shortly after Operations Successfully Performed on Adults for Congenital Blindness.—KOENIGSBERG, Orenburg (translated from the Russian by Carrick in the *Scot. Med. and Surg. Journ.*, July, 1902), made a study of what was actually recognized by the sight alone in three subjects successfully operated for congenital cataract at the ages of sixteen, eighteen, and twenty-eight years, respectively. In each case the most familiar objects could not be recognized until they had been touched. After they had been learned by the sight, sight alone was adequate for their subsequent recognition. The appreciation of space and distance was only attained after prolonged practice. On the other hand, objects were seen from the first as they are, and not reversed in spite of their being so imaged upon the retina. When a cylinder with concentric bands of different colors was shown, the patients at once named the respective positions of the bands. On asking the subject of the experiment to touch the upper part of the cylinder the hand was quickly stretched to that point, and the same test was employed in defining the lower part of the cylinder and with a like result.

The Nerve Supply of the Lacrymal Gland.—PARSONS (*Royal London Hospital Reports*, May, 1902) reviews the anatomical, histological, embryo-

logical, physiological, and pathological evidence of, and records some further observations upon, the nerve supply of the lacrymal gland. It has generally been considered that the secretory nerve fibres to the gland are derived from the fifth nerve. Some observers, reasoning principally from analogy with the salivary gland, have included the cervical sympathetic as an additional source of supply. More recently the seventh has been alleged to be the secretory nerve, and not the fifth. The writer inclines to this view, while admitting that the question is not yet settled.

Sympathetic Inflammation Affecting the Posterior Part of the Uveal Tract.—Fisher (*Royal London Ophthalmic Hospital Reports*, May, 1902) refers to two main classes of sympathetic ophthalmia. Of these iridocyclitis forms by far the larger; the other constitute but a small fraction. The latter are invariably called cases of neuroretinitis or papilloretinitis.

The prognosis in these cases is much better than in inflammations of the anterior uvea. Fisher thinks that it is the posterior uveal tract and not the nerve and retina which is primarily affected. In this condition the chorio capillaries might still retain a sufficiently free circulation to allow the retina which it helps to nourish to regain its full function, which is hardly to be expected in true inflammation of that structure. He reports a case.

Treatment of Incipient Cataract by Collyria and Ocular Baths of Iodine.—Badal (*Journ. de Med. de Bordeaux*, No. 29, 1901) has used collyria of sodium or potassium iodide in the strength of 1 : 250 for the collyria and 1 : 40 for the baths in incipient cataract; one or two drops of the collyria to be dropped into the eye morning and evening; the baths to be used twice a day in an eye cup. He has never seen any cataract become retrograde as a result of the treatment; but he affirms that in certain cases development has been arrested, and in a still larger number the progress has been unusually slow.

Treatment of Diphtheritic Conjunctivitis by the Instillation of Antitoxin into the Conjunctival Sac.—Chesneau (*Gazette Med. de Nantes*, February 15, 1902) reports upon the instillation of Roux's serum, every two hours in two drop-doses, into the palpebral fissure, in alternation with lemon juice. Eleven children, between the ages of fifteen months and two years, were so treated, with the most satisfactory results. Upon the second, or at latest the third day, the swelling of the lids went down, the folds in the skin reappeared, and the false membrane was reproduced only in spots. In four or five days the disease had become simply a common catarrhal conjunctivitis, which rapidly recovered. Of prime importance was the absence of corneal complications in this series of cases.

Tuberculous Dacryoadenitis and Conjunctivitis.—Stieren, of Pittsburg, Pa. (*Johns Hopkins Hospital Bulletin*, November, 1901), reports a case of tuberculosis of the lacrymal gland and ocular conjunctiva, with a review of the literature—twelve other reported cases.

Notwithstanding the great prevalence of tuberculosis, the eye enjoys greater freedom from tuberculous invasion than any other part or organ.

This immunity is due to the fact that the eye is almost constantly exposed to a lower degree of temperature than that in which the tubercle bacillus thrives, is very often exposed to the direct sunlight, is constantly bathed in and flushed by the tears, and expulsion of germs from the conjunctival sac is aided by the movements of the lids. The epithelial structure of the exposed parts of the eye, resting on a basement membrane, affords very little opportunity for invasion and growth.

The case reported occurred in a colored girl affected with general tuberculosis. The growth disappeared almost entirely without surgical intervention, this having been refused. The discharge and curettings were examined for tubercle bacilli, but always with a negative result.

The author's conclusions are:

1. Tuberculosis of the conjunctiva may be either ectogenous or entogenous; tuberculosis of the lacrymal gland must be hematogenous.

2. The presence of the tubercle bacillus in tuberculous conjunctivitis and tuberculous dacryoadenitis is not a *sine qua non* of the diseases.

3. Tuberculous conjunctivitis and dacryoadenitis may undergo cure. Surgical intervention is indicated only after therapeutic and proper hygienic measures fail.

HYGIENE AND PUBLIC HEALTH.

UNDER THE CHARGE OF

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Causation of Beriberi.—In the July number of this JOURNAL (p. 84) were given certain facts pointing to decorticated (white) rice as a cause of beriberi. Additional evidence that the disease is of alimentary origin is given by DR. ARTHUR STANLEY (*Journal of Hygiene*, July 1, 1902, p. 369), who shows that, in Shanghai, the Chinese prisoners under municipal police supervision are attacked more extensively than is the general public. The incidence in four widely separated prisons, completely isolated in every respect, was of approximately the same degree, but greatest where the length of incarceration was most prolonged, namely, at the jail. None of the European or Indian staff at these places was affected, although they resided in the same compound. This excludes soil and immediate surroundings as a cause. The fact that the disease occurs mainly among natives aggregated for periods longer than one month favors the idea of its propagation by contagion. Again, the operation of the infective agent, whether conveyed in food, or by parasites or by contagion, would be favored by aggregation of potentially infective units. The food supply of

three of the four prisons was from different sources, but the rice in use at all four was found to be of poor quality, weevilly, and mouldy. A change was made in the rice at all the prisons; an excellent quality of Annam rice was procured at an increased price. From the beginning of August the new rice was given out every three days. Toward the end of September, the number of cases diminished markedly, and in October they ceased. In spite of this fact, and because of a to-be-expected seasonal diminution, Stanley says the "results of the rice experiments were, therefore, probably negative," which finding would suggest that whoever chose that particular time for experimentation had not all of the qualifications of a true scientific investigator.

Stanley, in spite of an evident disinclination to believe in the rice theory, mentions the following facts, which certainly support it: In Japanese prisons beriberi has become a rarity since the daily allowance of rice was changed to a mixture of barley and rice in the proportion of 6:4. In 1899, the prisoners at Nugata were fed on Chinese rice, and from January to March, 400 of their number (1000) had beriberi. Those supplied with white (decorticated) rice were affected more extensively than those supplied with red rice. In Corea, where the Japanese and Coreans live side by side, the former eat rice and have the disease, and the latter live chiefly on peas, without rice, and escape. In the Straits Settlements, the Tamils decorticate their rice after it is cooked, and have very few cases of beriberi; while the Chinese and Malays eat rice that has been husked a year or longer, and suffer extensively.

From a series of sixteen conclusions with which Stanley's paper terminates the following may be quoted as having a bearing on the theory of alimentary origin:

6. Inasmuch as, apart from rice, the food supply of three out of the four prisons was from different sources, and a change of rice for all the prisons to one of recognized good quality produced no well-marked effect on the prevalence of the disease in two months, food infection would appear not to be a factor in the cause.

7. Beriberi being a peripheral neuritis, which is a pathological condition usually associated with toxæmia, food would, in the absence of a primary lesion (as in diphtheria), seem specially indicated as a cause. For the same reason the cause would be met with in specifically contaminated food rather than in either qualitative or quantitative changes in diet.

8. The marked and apparently primary degenerative action of beriberi on heart muscle, like that produced by diphtheria, and to a less degree by influenza and alcohol and arsenic poisoning, all of which may also cause peripheral neuritis, and the remarkable clinical resemblance of beriberi to diphtheria in the frequency of death from sudden heart failure, would also indicate a form of chronic poisoning.

9. The identity of the pathological changes in beriberi, diphtheria, and arsenic and alcohol poisoning, and the grouping of alcoholic poisoning with ergotism, pellagra, and lathyrism, which are caused by poisons produced by parasites in vegetable foods, suggest the possibility of the cause of beriberi being a toxin derived from an extraneous parasite of some article of food.

11. The oft-repeated statement that a beriberi patient recovers quickly when removed to a fresh locality may not indicate that this disease is a place infection, but rather that the source of the toxin may be removed by change of residence.

13. Something more is required for the prevention of beriberi than attention to the general rules of sanitation, such as ventilation, cleanliness, and diet. Moreover, isolation of cases as they arise, followed by disinfection, does not suffice to limit the disease.

14. The maximum incidence of beriberi in Shanghai being at the end of the tropical summer (the remainder of the year being quite temperate), the liability to recurrence yearly at this season in the same patient would be compatible with the elaboration of a toxin favored in its origin by the period of maximum atmospheric heat and moisture.

The Presence and Vitality of Bacteria in Oils.—Dr. Baldas (*Gironale della Reale Soc. Italiana d'Igiene*, February, 1901) notes that while surgeons are careful to secure the complete sterilization of all the water they use in the performance and subsequent treatment of operations, the possibility of oils and fats applied as vehicles of drugs to the absorbent and denuded surfaces of wounds and burns or to mucous membranes being the means of introducing septic or even pathogenic microbes does not appear to have been thought of. Dr. Baldas, impressed by the fact that the tubercle bacillus, and more often pseudotuberculous bacilli, had been detected in butter, began by examining the fats and oils most used in commerce and freely exposed to contamination from the air, and next those used in medicine and surgery. He found in these many of the hyphomyceti, of which the penicillium glaucum was the most frequent; the schizomyceti occurred more rarely, and he failed to discover any pathogenic germs in the crude oils. But as their absence in the samples in question was no proof that they might not be introduced, he proceeded to the experimental sowing of the oils with various pathogenic bacteria. When the oils were heated to considerable temperatures the germs rapidly disappeared, but at ordinary temperatures they retained their vitality unimpaired for two months, the duration of his observations. He did not employ the B. anthracis on account of its exceptional vitality, but he found that the B. coli, Eberth's bacillus, and the staphylococcus aureus and albus lost none of their vitality and virulence.

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DISEASES OF THE PANCREAS.[1]

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The pancreas is situated in the epigastric and left hypochondriac regions, on the body of the first lumbar vertebra, and from its protected position is less liable to injury and also less accessible to surgical manipulation than the other abdominal organs. Ashhurst quotes a table of 868 cases of injury to the solid viscera of the abdomen, of which only 1.5 per cent. were injuries to the pancreas. It is an elongated organ, measuring from 12 to 20 cm. in length, 4 to 5 cm. in width, and weighs from 60 to 100 grammes. It is pinkish in color and soft in texture, and may conveniently be divided into the head, neck, body, and tail.

Glinski has pointed out anomalies of the pancreas due to disturbances during development, and notes several forms of accessory and divided pancreas. An annular deformity, with resulting constricture of the duodenum, has been observed by Tieken.

The pancreas is a racemose gland made up of numerous lobes and lobules held together by a connective tissue framework and closely resembling the parotid gland in its structure. The secreting glands and acini are composed of high columnar cells becoming lower in the smallest ducts and again columnar in the larger ducts, which unite and empty into the pancreatic duct of Wirsung.

Langerhans, in 1869, after a careful study of the pancreas of rabbits, which closely resembles that of other mammals, described groups of cells, irregularly polygonal and having a round nucleus situated in the

[1] Read before the West Penn Medical Society, Pittsburg, November 25, 1902.

parenchyma of the lobules; these are termed the "islands of Langerhans." They are of the same origin as the glandular acini, but are independent of them, and have an intimate relation with the vascular system, the capillaries forming a network with a tortuous course and resembling the glomeruli of the kidney. The "islands" are three and a half times more numerous in the tail of the organ than in other portions, and probably have some special function, imperfectly understood as yet, but probably having some relation to carbohydrate metabolism. Lewaschew claimed that he could increase their number by overstimulation of the gland with repeated injections of pilocarpine and by overfeeding, and that this increase took place at the expense of the acini; but Opie by a series of careful experiments on dogs found that prolonged stimulation does not transform groups of acini into "islands of Langerhans."

The relation of lesions of the pancreas to diabetes is of great interest, and Opie and others have found marked changes in the "islands of Langerhans" in this connection without any alteration in the parenchyma of the gland.

The pancreatic or Wirsung's duct commences near the tail of the pancreas and passes from left to right, becoming larger as it receives the tributaries, and at the neck of the gland turns slightly downward and backward, and unites, near the head of the pancreas, with the common bile-duct, and they together form the ampulla of Vater, which empties by a narrow opening into the posterior surface of the duodenum, about three inches from the stomach. In nearly every instance a second or accessory duct is present—Santorini's duct. This leaves the main duct before its union with the bile-duct, passes behind the latter, and is continued forward into the duodenum, about two inches from the stomach and about one inch above the opening of the diverticulum of Vater. Schirmer in a study of 105 anatomical specimens found that in all but 2 instances some evidence of a second duct was present, and that in 53 per cent. of the cases this accessory duct was capable of draining the pancreas, and at the same time was not subject to stoppage by gallstones. Bünger found an accessory duct in only 10 per cent. of 58 cadavers examined.

The diverticulum of Vater is about 8 mm. in length, conical in shape, with the apex opening into the duodenum on a longitudinal fold of mucous membrane, and the two ducts opening into the base rather nearer the posterior than the anterior wall. Bünger, however, states that in 98 to 99 per cent. of his 58 examinations the two ducts did not unite, but opened at separate points in the duodenum, and that, as a rule, the pancreatic passed beneath the bile-duct.

These anatomical peculiarities are interesting because of the etiology of pancreatitis. Opie makes the following statement in reviewing a

case of Halsted's: "A small gallstone impacted in the diverticulum of Vater may occlude the common orifice of the bile-duct and duct of Wirsung and convert them into a continuous closed channel. Bile enters the pancreas by way of the pancreatic duct, and the pancreas becomes the seat of inflammatory changes characterized by necrosis of the parenchymatous cells, hemorrhage, and the accumulation of inflammatory products. Anatomical peculiarities of the diverticulum of Vater do not permit this sequence of events in all individuals."

The pancreas holds a relation to many important structures, and the severity of the symptoms when it is attacked by disease is undoubtedly due to this relation. The head is in intimate relation to the curving duodenum and to the superior mesenteric vessels, and is crossed by the transverse colon. Sometimes a prolongation reaches the lesser curve of the stomach. The body is in contact with the stomach anteriorly, and with the diaphragmatic crura, vena cava, aorta, superior mesenteric vessels, left kidney, and suprarenal gland posteriorly. It is also in relation with the cœliac axis, solar plexus, and splenic artery. The tail is in contact with the anterior surface of the spleen.

The blood supply of the pancreas is derived from the splenic, hepatic, and superior mesenteric arteries, and is returned into the portal system.

The lymphatics terminate in glands lying on the splenic and superior mesenteric arteries and between the pancreas and spleen and pancreas and duodenum.

Branches from the solar plexus furnish the nerve supply.

The peritoneum is derived from a reflection of the transverse mesocolon.

The secretion from the pancreas is clear, alkaline in reaction, with a specific gravity of about 1030, and contains four ferments, trypsin, amylopsin, steapsin, and a milk-curdling ferment. Steapsin is the fat-splitting ferment and is frequently a factor in the production of fat necrosis. Baker, in 1882, was the first to describe this condition, which has since been investigated by Langerhans, Hildebrand, Flexner, Opie, Korte, and others, and has furnished a fertile field for experimental study. By fat necrosis is meant the action of the pancreatic secretion upon surrounding fat areas and the splitting of this fat into fat acids and glycerin, and the combination of the fatty acids with lime salts with the resulting formation of whitish patches in the omentum, mesentery, and subperitoneal fat, and occasionally in the pericardial or subcutaneous fat as well.

In experimental work fat necrosis has been produced by ligating the pancreatic duct in animals and stimulation of the pancreas by pilocarpine. The animals lived for twenty or thirty days after the operation, thus allowing the pancreatic secretion to penetrate for some distance, and both Opie and Flexner have obtained fat necrosis of the

epicardial fat in this way. Associated with the fat necrosis, hemorrhage of the pancreas has usually been observed, and the action of the glycerin set free has been ascribed as the cause, but proof as yet is wanting.

The pancreas is rarely injured, owing to its protected situation, but this occurs occasionally as the result of blows upon the abdomen or from behind, and gunshot or stab wounds. The late President McKinley was wounded in the pancreas indirectly, and the organ became necrotic in part, though no fat necrosis occurred.

The injury will be followed by rapid onset of shock and early collapse, and, if the pancreas alone is injured, little bleeding follows. The combination of the digesting action of the pancreatic ferments with a bacterial infection from the wound itself necessitates immediate operation and the repair of the injured organ; but in most cases other viscera, like the spleen or liver, are involved, and severe hemorrhage makes the prognosis far from hopeful. Injury of the pancreas which is not so severe as to cause rupture may induce the formation of inflammatory cysts, especially into the lesser peritoneal sac, with the foramen of Winslow closed by inflammatory process. These tumors form with great rapidity. Chronic pancreatitis may follow bruising or result from injury to the pancreas during operations upon the stomach or biliary passages, when, from the difficulty of the operation, the pancreas has been excessively handled; therefore, these operations should be done with the greatest care and gentleness. Prolapse of the pancreas through an abdominal wound is rare, but has been recorded several times. Robson has collected eight such cases from the literature.

In February, 1889, Reginald Fitz, of Boston, delivered the Middleton-Goldsmith Lecture for that year upon the subject of "Acute Pancreatitis." The service he rendered to the medical profession may be judged from the fact that every subsequent writer upon this subject has acknowledged his indebtedness to Fitz for the impetus which that celebrated internist gave to the pathology and treatment of the disease.

Until 1842 the subject of pancreatitis was mostly discussed from a theoretical standpoint, and such views as prevailed associated the diseased pancreas with mercurial poisoning.

Classen, in 1842, collected six cases which he regarded as probable pancreatic disease that had resulted fatally, and described the symptoms of the disease from these cases. As Fitz points out, the correctness of the diagnosis of these cases is very doubtful.

Klebs, Friedrich, and Balser published valuable contributions to the subject, and Balser, in 1882, called attention to the presence of areas of fat necrosis associated with pancreatic disease. Senn, in 1886, published his classical work on the surgery of the pancreas, and in 1889

Fitz accurately described and classified acute pancreatitis, advising palliative treatment in the early stages, and suggesting surgical treatment in the suppurative and gangrenous forms.

In 1895 Birch-Hirschfeld described chronic pancreatitis, and Schlessinger, in 1898, investigated this condition further. In 1900 Mayo Robson, in a lecture before the London Polyclinic, pointed out the surgical importance of chronic pancreatitis, and called attention to the similarity which it bore to cancer of the pancreas.

The etiology of pancreatitis is still obscure. It seems to be a disease of the middle period of life of high-livers, and more especially when a free use of alcohol is indulged in, and in those who have a tendency toward corpulency. Gastroduodenal catarrh, with extension to the duct, and followed by bacterial invasion, may be a factor, and as the duodenum from its contour will aid in the delay of any decomposing food products, this factor should be seriously considered.

Ulcer and cancer of the stomach, pylorus or duodenum and zymotic disease, such as enteric fever, mumps, and influenza, are the determining factors stated by Mayo Robson.

Biliary and pancreatic calculi are certain causes of pancreatitis. The association of gallstones with pancreatic disease has been repeatedly observed and recorded, and the impaction of a stone in the ampulla of Vater at its orifice will cause the penetration of bile into the pancreatic ducts and an acute pancreatitis. This has been observed clinically and produced experimentally.

Pancreatitis may be divided clinically into acute, subacute, and chronic.

Acute pancreatitis is characterized by the sudden onset of pain in the epigastrium, colicky in nature, accompanied by prostration and anxiety. Vomiting is an early symptom, and, as a rule, is severe. Examination of the abdomen reveals a tender swelling in the epigastrium, tympanitic upon percussion. Constipation develops, and is so difficult to overcome that acute intestinal obstruction has frequently been made as the diagnosis. Collapse may rapidly follow, with a distending and rigid abdomen, small, rapid pulse, irregular temperature, delirium, and death. In these cases the pancreas is found to be the seat of an acute cellular or fibrinocellular infiltration of the connective tissue of the organ, with a more or less extensive necrosis of the lobules, and with diffused hemorrhage into the organ; fat necrosis, if present, is not widely distributed; a blood count is useful in determining the amount of hæmoglobin. In the less acute cases life may be prolonged for days, and recovery sometimes occurs.

The diagnosis of acute pancreatitis is attended with difficulty, owing to the obscurity of the symptoms, which are mainly those of acute peritonitis originating in the epigastrium. Intestinal obstruction is

the usual diagnosis made, and in fact the two may coexist, as Robson points out, from strangulation of the duodenum by inflammatory material or by the swollen pancreas itself. The obstruction, however, is not so absolute, and repeated enemas, before peritonitis has supervened, finally restore the peristalsis of the bowel. In favor of intestinal obstruction is the slow pulse, normal or subnormal temperature, the more general and usually greater degree of abdominal distention, inability to stool or pass flatus, vomiting persistent, soon becoming stercoraceous. Palpation of abdominal walls excites storms of pain. In favor of pancreatic disease is the history of previous attacks. In perforating gastric or duodenal ulcer the tenderness to pressure is not so acute, and there is less muscular rigidity in the early stages. The early bowel paresis will raise the lower border of liver dulness in ulcer, and there are also the premonitory symptoms of gastric pain associated with taking food, the occasional vomiting of blood if the stomach or the first portion of the duodenum be the seat of the ulcer, black stools, if the ulcer be in the lower portion of the duodenum, and the chlorotic tendency.

In cholecystitis the pain is never as severe, and is located over the gall-bladder, radiating to the right shoulder, breast or back, while in pancreatitis, if radiation occurs, it tends to go toward the left. There is usually a history of enteric fever and gallstone attacks. Rigidity is less general and early distention seldom present.

Acute ptomaïne poisoning may resemble pancreatitis, but the more general nature of the colic, the constant diarrhœa, and the previous history should decide the diagnosis.

The treatment of pancreatitis is still open to discussion. Many of the milder cases recover without operation, but, on the other hand, the majority of the severe acute cases rapidly collapse, and may die without a diagnosis having been made. Definite rules for treatment cannot be laid down, but to each case the judgment of the surgeon must be applied.

In the less severe type of cases the patient should be put at absolute rest, giving sufficient morphine to quiet the pain, which is always very severe, combating depression by the use of stimulants, especially enteroclysis, combining whiskey with the salt solution. The vomiting may be relieved by lavage and rectal feeding, and for the feeling of oppression in the epigastrium hot fomentations or turpentine stupes may be applied.

In cases which are more severe the abdomen may be opened and gauze drainage introduced. The hemorrhagic form of pancreatitis may be accompanied by necrosis and disintegration of gland tissue, and such conditions are best treated by a free incision and gauze drainage. In this form of pancreatitis the anæmic condition of the patient, as in extra-uterine hemorrhage, may be marked.

In the very severe cases the extreme shock will contraindicate operation and require every possible stimulation to save the life of the patient. Death is often a matter of hours from the onset of the initial acute symptoms.

The following cases occurred during the past two years at the German Hospital:

Mrs. C. S., aged twenty-seven years. Family history of tuberculosis. Previous history negative, except for habitual constipation and the free use of alcohol of recent years. Three weeks before admission the patient was exposed to cold and wet, and became acutely jaundiced, with pain across the back, and nausea and vomiting. It lasted a few days and she then improved. This was probably an attack of alcoholic gastroduodenitis. The jaundice subsided. Eight days before admission she was suddenly seized with pain throughout the abdomen, most marked on the right side, high up. No vomiting, but bowels were constipated. The pain continued until her admission to the German Hospital.

On admission the patient was anæmic-looking, with yellow scleræ. Temperature of 101°; pulse, 120. The abdomen was slightly distended and tender all over, with a point of greatest intensity one inch above and one inch to the right of the umbilicus. Gall-bladder tender, but not enlarged. Spleen was slightly enlarged. No mass could be detected. The X-ray showed the absence of a pathological shadow. The urine contained a trace of albumin, but no sugar or casts. There were 24,400 leucocytes to the cubic millimetre. Vaginal examination negative. On the day after admission she vomited large quantities of a greenish material, and the leucocytes rose to 32,800. Vomiting continued for twenty-four hours, and was then relieved by gastric lavage.

Six days after admission she was much better, the abdomen was flat, and no pain or tenderness except an occasional colic about the umbilicus. Leucocytes were still high, 21,600; twelve days after admission she was up and about the room, with a normal temperature and blood count, and no pain of any kind.

Mrs. M. C., aged fifty years. No family or previous personal history was obtained. Patient was admitted to the hospital in a state of collapse, with subnormal temperature, rapid and feeble pulse, cold, clammy skin, and cyanosis.

The abdomen was distended, rigid, and tender throughout, with very intense colicky pain in the epigastrium. Death took place six hours after admission. From her relatives it was elicited that twenty-four hours previous to admission she had been suddenly seized with violent epigastric pain, nausea, vomiting, and diarrhœa. There was no alcoholic history. The woman was quite stout. Post-mortem revealed a diffused fat necrosis of the omentum and mesentery, which in some places had broken down and undergone calcareous degeneration. The pancreas was enlarged and hard, with a hemorrhagic appearance on section. No gallstones were present.

As has been stated, hemorrhage into the pancreas may cause foci of necrosis, and when this process gradually increases, with larger areas

of coagulation, necrosis and sequestration of portions of the gland, the condition of necrosing pancreatitis exists.

Gangrenous and suppurating pancreatitis are due to the invasion of the gland with micro-organisms, and are accompanied, as a rule, by widely disseminated fat necrosis. The gangrenous form is probably a later result of hemorrhagic pancreatitis, and the pancreas may be dry, black, and necrotic.

Suppurative pancreatitis may coexist with the necrotizing form, and is characterized by purulent collections in the parenchyma or interstitial tissue of the gland, with sometimes a general infiltration. Such abscesses may form peripancreatic collections and rupture into the stomach, duodenum, or colon. Thrombus of the portal vein and infection of the liver may follow the extension of infection.

The symptoms of the suppurating and gangrenous forms of pancreatitis are marked by the usual sudden onset, with intense pain, vomiting, and shock, followed by septic symptoms, with, perhaps, delirium. Palpation elicits the most valuable symptom—a tender mass in the epigastrium. The continuance of the symptoms observed in many of these cases allows time for a thorough examination of the stools for fat or evidence of imperfect digestion. The urine may show evidence of glycosuria and, therefore, disease of the islands of Langerhans. The presence of the fat-splitting ferment of the pancreatic juice has not been clearly demonstrated in the urine, and the success of such a test would be a valuable sign in the diagnosis of the disease. Reduction in the amount of ethereal sulphates in the urine is an inconsistent sign of pancreatic disease, but has not been sufficiently tried as yet.

The treatment of the suppurative and gangrenous form of pancreatitis consists in laparotomy, evacuation of pus and drainage of the purulent foci. The following case occurred a few days ago in the German Hospital:

Mr. T., aged fifty-two years. Family history negative. Had ordinary diseases of childhood. Malaria, typhoid fever twenty-six years ago, and rheumatism. Uses alcohol and tobacco moderately. Bowels irregular, and digestion fair, some tendency toward dyspepsia. Twenty-five years ago he had an attack of colicky pain in epigastrium, with vomiting; no jaundice. Lasted twenty-four hours, and the pain during that time was very severe. Has had four attacks similar to this. Three days before admission he had a slight colic in epigastrium, vomiting, dyspeptic symptoms, like belching and nausea, and noticed that his abdomen was distended and the stools clay-colored. On the day before admission had a sharper attack of vomiting of a clear, green, bile-stained material.

On admission the patient is a heavy, stout man, with yellow scleræ, coated tongue, muddy skin, and a distended and tympanitic abdomen. This distention is most marked in the epigastric region, at which local-

ity considerable tenderness could be elicited on palpation. He complained of pain across the lower thorax, which was accentuated by coughing, during which time acute pain was felt over the abdomen. The urine showed the presence of albumin, casts, and bile, but no sugar. The blood indicated an anæmia and 8200 leucocytes. The stools contained free fat. An X-ray gave a shadow dense in character and over the region of the pancreas.

The patient was kept at rest for a week after admission without any change in his symptoms being observed. The temperature remained between 100° and 101° F., the pulse about 90, and respiration at 28.

On the day before operation there were 13,850 leucocytes counted with 81.3 per cent. of the polynuclear type and 18.7 per cent. of the mononuclear type. There were no eosinophiles observed. Vomiting ceased under treatment, but the strength of the patient was rapidly failing, and operation was decided upon. No mass could be felt at any time in the region of the pancreas, but there was a sense of resistance over the gall-bladder and pancreatic regions, with marked tenderness.

Operation under ether anæsthesia, which was administered with difficulty owing to the cyanotic condition of the patient. An incision was made through the left rectus. The omentum was observed to be speckled with areas of fat necrosis, and the epigastrium was the seat of a peritonitis. The gastrocolic omentum was opened with the fingers and the lesser peritoneum found to be full of a chocolate-like material. This was mopped out with sponges and rubber, and gauze drainage passed down to the bottom of the cavity. The patient's condition forbade any further interference, and he was sent back to bed. Death occurred three hours later.

As no autopsy was permitted the operative wound was merely opened and slightly enlarged. Diffused fat necrosis was found in the omentum, mesentery, and peritoneal fat. The meso-appendix and the epiploic appendages were involved. There were many areas of calcareous infiltration, some of which had broken down. On widely opening the gastrocolic and gastrohepatic omenta and raising the stomach the pancreas was found to be necrotic, black, and gangrenous throughout its entirety, with the exception of the head, which, while apparently diseased, was not gangrenous. The entire fat of the lesser peritoneum and adjacent structures, including the peritoneal fat, was in a state of necrosis and mostly liquefaction necrosis. The spleen was slightly enlarged. The gall-bladder was distended and filled with gallstones, many of which were small, and the cystic duct was occluded by a stone. The liver appeared normal. The common duct was free from a stone as far as could be determined, though its course in the pancreas could not be found. The ampulla of Vater was clear. The pancreatic duct could not be made out. No further post-mortem examination could be made. Cultures were taken from the region of disease, and are being studied.

Subacute pancreatitis will present the general symptoms of the more severe type, but in a lessened degree. The onset is more gradual, the pain is less severe, and the vomiting is not so violent. The case is more prolonged and the primary constipation is frequently succeeded by diarrhœa, with pus or blood in the stools. The temperature is more

elevated, as a rule, and the depression is markedly lower. The patient in the fatal cases gradually loses strength and weight, or may show evidences of severe septic poisoning. If an abscess develops, a tender tumor mass may be palpated in the epigastrium.

The treatment of subacute pancreatitis has been described, and will vary with the severity of the symptoms and the presence or absence of suppuration.

Chronic indurative pancreatitis is probably a more common disease than the number of reported cases seems to show, and many of those cases diagnosed as malignant disease of the head of the pancreas are probably of this character.

Opie's conclusions, after a study of twenty-nine cases of chronic pancreatitis, define the present status of the etiology and pathology of the disease:

"1. Chronic interstitial pancreatitis is slightly more frequent in males than in females. Two-thirds of the total number of cases occur between the ages of forty and sixty years. 2. The most frequent cause of chronic pancreatitis is obstruction of the duct of Wirsung, due to pancreatic calculi, to biliary calculi in the terminal part of the common bile-duct, or to carcinoma invading the head or body of the gland. Duct obstruction may be followed by the invasion of bacteria, which take part in the production of the resulting lesion. 3. Ascending infection of the unobstructed duct of Wirsung may follow an acute lesion of the duodenum or of the bile passages, and may cause chronic inflammation. In cases which have given a history of long, persistent vomiting, chronic diffuse pancreatitis may be found at autopsy, and is probably the result of an ascending infection of the gland. 4. General or local tuberculosis is occasionally accompanied by chronic diffuse pancreatitis, affecting chiefly the interstitial tissue of the gland. 5. Chronic interstitial pancreatitis is not infrequently dependent upon the same etiological factors, notably alcohol, which produce cirrhosis of the liver, and in about one-fourth of the cases the two lesions are associated. 6. Following duct obstruction and ascending infection, the lesion affects principally the interlobular tissue, only secondarily invading the lobular tissue and sparing the islands of Langerhans. Diabetes results only when the lesion is far advanced. 7. Accompanying the so-called atrophic or Laennec's cirrhosis of the liver the pancreas is sometimes the seat of diffuse chronic inflammation, characterized by diffuse proliferation of the interacinar tissue, which invades the islands of Langerhans. A similar lesion accompanied hyaline degeneration of the islands of Langerhans and the condition known as hæmochromatosis. 8. Interacinar pancreatitis is usually accompanied by diabetes mellitus. When diabetes is absent the lesion is of such slight intensity that the islands of Langerhans are little implicated."

The diagnosis of this condition is rather difficult to make because of the usual gradual and painless onset. In some cases the initial symptoms resemble those of a gallstone attack, with pain, vomiting, and jaundice. The pain is more in the epigastrium, however, and may be referred to the left side or backward to the midscapular region. The greatest point of tenderness will be found one inch above and one inch to the right of the umbilicus. When the induration of the head of the pancreas is sufficient to obstruct the bile-duct jaundice slowly deepens and becomes chronic. There is usually rigidity of the recti muscles. Asthenia is a constant symptom, and dyspeptic symptoms and frequently diarrhœa will be noted. In the later stages the cachexia, the tumor which may be palpated in the epigastrium, and the enlarged gall-bladder present a picture which is very difficult to diagnose from that of malignant disease.

In all of Mayo Robson's cases numerous adhesions were found around the duodenum, pylorus, and hepatic flexure of the colon, and even occluding the foramen of Winslow and adherent to the gall-bladder and liver.

Later sequelæ may result, such as gastro-ectasis, abscess of the liver, ascites, and intestinal obstruction from the constricting adhesions.

The differential diagnosis must be made from gallstones, malignant disease of the pancreas, liver, and biliary passages, and chronic gastritis.

The diagnosis of gallstones is not very important, as both diseases require a surgical operation.

The previous history of repeated attacks of colic, intermittent jaundice, the absence of enlargement of the gall-bladder, and the location of the tenderness to palpation, with the direction of the referred pain, will often indicate the diagnosis.

From carcinoma of the pancreas the diagnosis, as has been said, is difficult and seldom made. The more marked cachexia, the absence of pain or tenderness, enlargement of the gall-bladder, normal temperature, extreme jaundice, ascites, and the enlarged, smooth liver are the usual symptoms observed in malignant disease. When the liver is involved nodular masses may be palpated.

Chronic gastritis, especially when it is associated with catarrh of the duodenum or biliary passages, has been mistaken for chronic pancreatitis; but active medical treatment should soon relieve the symptoms which resemble those of the pancreatic lesion.

The treatment of chronic pancreatitis consists in the relief of tension by opening and draining the gall-bladder, with the formation of a biliary fistula. Cholecystostomy is the operation to be preferred to the former method of cholecystenterostomy.

The following cases of chronic pancreatitis occurred at the German Hospital recently.

E. O., aged forty-four years. Family history is negative. During early life he had measles, whooping-cough, scarlet fever, varicella, mumps, and diphtheria; but since twelve years of age has enjoyed almost perfect health until 1890, when he had an attack of diarrhœa lasting for nearly four years, more or less severe in character. Appetite is always good, and no dyspeptic symptoms have been experienced. He smokes five or six cigars daily, uses alcohol moderately, and is a man of very good habits.

In 1891 he had a sudden and severe attack of pain in the epigastrium, lasting two or three hours, then passing downward throughout the abdomen, and followed by diarrhœa; no vomiting. The pain was colicky in nature, and usually relieved by sinapisms. A number of attacks recurred at intervals of six months. In July, 1901, he had an attack similar to the preceding, but more severe in character; it lasted about two hours, and was relieved by the application of a strong red-pepper plaster; no vomiting. After this attack he enjoyed exceptionally good health until June, 1902. Owing to overwork, he became depressed and nervous. His physician found that his heart action was weak and irregular, and prescribed rest. Œdema of the feet was present, and a urine examination excluded nephritis. He then became progressively weaker, with anorexia, and again suffered from diarrhœa and pain in the region of the epigastrium, colicky in nature, but nearly constant. There was a sensation of bloating present. During the week previous to admission there was constant epigastric pain, with marked constipation and with rectal tenesmus and desire to have a bowel movement, without result. No nausea or vomiting; no urinary symptoms.

On admission the patient is flabby and rather stout, with a pale skin of a dull, ashen color. Scleræ are yellow, tongue is coated, and breath is foul. Pulse is rapid, and the patient is markedly nervous. Heart is weak, with a tendency to irregularity. The lungs are clear, and no apparent enlargement can be made of the liver, gall-bladder, or spleen. There is no albumin, sugar, or biliary coloring-matter in the urine. The epigastrium is tender and the abdomen distended. No palpable tumor could be detected over the pancreas, but chronic pancreatitis was diagnosed.

Operation under ether anæsthesia revealed a hardened and enlarged pancreas at its head, without any fat necrosis. The bowels were carefully gone over from the sigmoid to the pylorus, and no obstruction bands found, nor was there any peritonitis beyond the early stages of hyperæmia. The gall-bladder was distended and somewhat enlarged, while the liver was light in color and probably fatty.

A cholecystostomy was performed, with the difference that the gall-bladder was sutured to the peritoneum and aponeurosis without opening it, and gauze drains were introduced not only around the gall-bladder, but to the space below the liver.

The patient reacted very well from the operation, and two days later the gall-bladder was opened with the actual cautery, and rubber drainage instituted. Seven days after operation part of the drainage was removed, and thirteen days after operation the remaining gauze was taken out. The patient then became rapidly convalescent.

S. Z., aged fifty-five years. One brother died of tuberculous enteritis. Measles, whooping-cough, influenza, and malaria. Bowels are

irregular and appetite good. Moderate user of alcohol. The attack of malaria occurred twenty years ago, and was accompanied by jaundice, lasting for three or four weeks, and colicky pain in the epigastrium, followed by irregularity of bowels and dyspeptic symptoms for some years. Six weeks before admission he was seized with severe pain in the epigastrium, colicky in nature, and referred to the umbilicus; one week later became jaundiced, with intense itching. Urine was dark, and stools became lighter. No vomiting.

On admission patient was markedly jaundiced, with a slow pulse. He was a large man, with considerable adipose tissue. Examination of abdomen: The liver is enlarged, but not tender. The gall-bladder is large, palpable, and very tender, and an X-ray revealed a dense shadow in the epigastrium, to the right of the median line. The urine contained albumin, casts, and biliary coloring-matters, but no sugar. The blood showed a marked anæmia, 5000 leucocytes, and delayed coagulation. There were no gallstones in the stools.

Operation was performed, under ether anæsthesia, eight days after admission. The gall-bladder was much distended and fluctuating and non-adherent; it was aspirated of 350 c.c. of thick bile and the opening closed with a hæmostat. No gallstones were detected in the gall-bladder, cystic or common ducts. The pancreas was found to be enlarged, hard, and infiltrated. A cholecystoduodenostomy was performed, using a small Murphy button. The wound was closed with silk tier sutures, and except for a small stitch abscess the patient made an uninterrupted recovery, and was discharged twenty-eight days after operation. His jaundice had nearly faded, and the stools were of a natural color.

J. C. K., aged fifty-eight years; a shoemaker by occupation. Family and previous personal history was negative. Used alcohol moderately. His position while at work caused occasional pains in the epigastrium, but never vomiting. He had never, to his knowledge, passed blood or gallstones in the stools. Six months before admission he suffered from weakness, anorexia, and coldness of the extremities, and was placed on a milk diet, which caused marked constipation. Three weeks later he became jaundiced, which deepened, but without pain other than an occasional colicky attack to the right of the epigastrium. He lost weight—twenty-three pounds—during the six months.

On admission the heart and lungs were normal, the spleen not enlarged. Temperature and pulse normal. He was profoundly jaundiced and emaciated. The urine contained a trace of albumin; no casts or sugar; a normal amount of urea; absence of indican and presence of bile. A stomach analysis showed a trace of hydrochloric acid, the presence of lactic acid, and a total acidity of 12. Boas-Appler bacilli were absent. The stools were negative for free fat or gallstones. A number of blood examinations revealed an anæmia, no leucocytosis, and delayed coagulation. The latter was not benefited by the use of calcium chloride for the four days preceding operation. An examination of the abdomen found the recti muscles rigid, especially in their upper quadrants. To percussion an area of dulness could be detected over the region of the pancreas and extending above and to the right and merging with the liver dulness. The inguinal lymphatics were enlarged. A fluoroscopic examination revealed a diffuse shadow around the head of the pancreas.

Operation was performed four days after admission, under ether anæsthesia. The gall-bladder was found to be small and adherent to the liver, with a large stone in the cystic duct. A cholecystectomy was done and a peritoneal cuff sewed over the stump. Following the common duct with the finger in the foramen of Winslow a round, hard mass could be made out, presumably a stone in the common duct near the duodenum. The abdomen was deep and examination difficult, but the common duct was dilated to three times its normal size. The duodenum was opened opposite the ampulla, and the obstruction was found to be the head of the pancreas; the duodenum was therefore closed and opened behind, and a choledochoduodenostomy performed, with silk suture. An incision was then made in the right loin and gauze disposed about the anastomosis, leading across the stump of the gall-bladder and thence under the liver and out the loin. A rubber tube and two wicks of gauze were used to drain from the anastomosis through the abdominal wound. Abdomen partly closed. The patient left the table in fairly good condition, with pulse of 72. There was a continuous capillary oozing, however, and the patient grew weaker, the pulse feebler, and death took place twenty-four hours after operation.

A post-mortem revealed a chronic pancreatitis, mitral insufficiency, nutmeg liver, and chronic congestion of the spleen and kidneys. There was no fat necrosis.

Pancreatic lithiasis is a condition difficult to diagnose. Chronic interstitial pancreatitis is usually associated, and dilatation of the duct and cyst or abscess formation may result. The symptoms resemble those of biliary colic, with radiation of the pain to the left side; rarely jaundice. Glycosæmia may be present, and the calculi have been recovered from the stools. If the condition be diagnosed the stone might be removed by opening the duct through the duodenum in the same manner that a biliary calculus in the common duct close to the duodenum is extracted.

Cysts of the pancreas have been observed and operated upon a number of times by surgeons. In Körte's recent monograph 121 cases are collected, of which 60 were in males and 56 in females. According to the origin he divides them into:

1. Traumatic, following blows or continued pressure upon the abdomen.

2. Post-inflammatory.

3. Cysts without any apparent exciting cause. In this class of cases the cysts existed for a very long time and caused but few symptoms. A cyst of this character occurred at the German Hospital during the present year, and will be discussed shortly.

Anatomically, Robson gives this classification:

1. Retention cysts.
2. Proliferation cysts; cystic adenoma or epithelioma.
3. Hydatid cysts.
4. Congenital cystic disease.

5. Hemorrhagic cysts.
6. Pseudocysts.

Retention cysts are due, as a rule, to plugging of the main duct or of the smaller ducts, with consequent dilatation of them and of the alveoli. They have been recognized during the course of operation by several observers.

Proliferation cysts are usually true glandular cystomata.

Hydatid and congenital cysts are very rare conditions.

Of hemorrhagic cysts Mayo Robson writes that "it may be stated with emphasis that there is no valid or acceptable evidence in favor of the hemorrhagic origin of these cysts; the tendency to bleeding, in greater or less degree, is observed in all pancreatic cysts, and the presence, therefore, of blood in predominant quantity is not sufficient to establish a hemorrhagic onset."

Pseudocysts are usually traumatic in origin or follow inflammatory affections of the pancreas, and are really accumulations of fluid in the lesser peritoneal cavity. Jordan Lloyd concludes that "when the contents of such tumors are found to have the property of rapidly converting starch into sugar we may assume that the pancreas has been injured."

The situation of pancreatic cysts is variable. Any part of the gland may give rise to them, but the tail is the most frequent site. The direction of the growth is also variable; the greater number, developing in the lesser peritoneal sac, push the stomach upward and to the right, and emerge between the stomach and transverse colon. In some cases the tumor reaches the abdominal wall above both the stomach and colon, pushing them downward; in other instances the cyst is below the colon and at the lower portion of the lesser sac, between the two layers of the transverse mesocolon. Occasionally the cyst extends in the direction of the spleen or the kidney. As a rule, the cyst is adherent to the surrounding structures, especially to the stomach, colon, duodenum, omentum, and anterior abdominal wall. Some cases are free from adhesions, and excision is easy.

As to the contents, Robson, quoting from Körte, concludes that the characteristics of a pancreatic cyst are "a blood-stained, reddish-brown or dark fluid, slightly viscid, alkaline, rich in albumin, of a specific gravity of 1010 to 1020. Ferments are frequently present, and when in pronounced quantity establish the diagnosis; their absence allows no conclusions to be drawn against the pancreatic origin of the cyst." The writer has observed the contents to be oily, and again to appear like sebaceous material.

The symptoms of a pancreatic cyst depend upon the pressure exerted. In neither of the cases herein reported was pain a symptom of any moment. Both patients complained of epigastric discomfort at times,

but no distinct pain. Vomiting is usually present, is more marked after eating, and is in direct proportion to the amount of pain suffered. Our two cases were free from pain, and never complained of vomiting. Constipation is the rule, and jaundice may be present and is dependent upon the obstruction to the common bile-duct. Wasting frequently results, with advancing weakness. The presence of sugar in the urine, fat and undigested proteids in the stools, and decolorization of the stools has been observed, but is not constant.

The differential diagnosis must be made from renal tumors, such as hydronephrosis, enlarged spleen, ovarian cysts, hydatid cysts of the liver, mesenteric cysts, retroperitoneal sarcoma, and large abdominal aneurisms. The previous history and slow onset, with progressive weakness; the deep situation of the tumor and its immobility; the condition of the stools; and, further, the fact that the great majority of cystic tumors in the epigastrium are pancreatic, should aid in the diagnosis. The treatment of cysts of the pancreas consists in abdominal section and removal when possible; or in case of extensive adhesions, or their having a broad basal attachment, incision, and drainage.

The following cases occurred at the German Hospital during the past three years:

Mrs. E. S., aged fifty-eight years. One brother died of tuberculosis. Previous history negative. Menopause at forty years of age. Her habits were good. Three years ago she had a "typhoid malarial" infection, as she termed it, which lasted for a number of months. The symptoms of this attack were but imperfectly described, but it evidently was a long and mild attack of enteric fever. A few years after the menopause she became stouter and corpulent, and has continued to slowly increase in the girth of the abdomen. Constipation was the rule, and occasionally she would have difficulty in micturition. She was sent to the hospital and the case diagnosed as ovarian cyst.

On admission the patient is a large and stout woman, with a circumference at the umbilicus of fifty-two inches. She suffers no pain. Examination of the abdomen revealed enlarged and tortuous superficial veins, general fluctuation, and deep-seated tympany in the right flank, and dulness, but not flatness, in the left flank. The anterior surface of the abdomen was flat to percussion, extending upward to the ensiform, and the area of dulness was not altered by any change in position. No outlines of a cyst or mass could be definitely made out, though there was a hard, cartilage-like body two inches below and two inches to the right of the ensiform, about 4 x 3 cm. in size and just beneath the abdominal wall. The lower border of liver dulness is displaced upward for two inches. The apex-beat is pushed slightly upward and to the left. Vaginal examination negative. The urine was free from albumin and sugar, and a blood count showed marked anæmia, with a normal leucocyte count.

Under ether an incision three inches in length was made in the median line above the pubis. On opening the peritoneum about

3000 c.c. of ascitic fluid were evacuated. It was then possible to determine that a large cyst was present in the upper abdomen, adherent to the anterior abdominal wall, colon, omentum, and other viscera, and by an adhesive band to the right broad ligament. The incision was continued upward to the ensiform, and the adhesions found so extensive that removal of the cyst was totally impossible. The lower three-fourths of the wound were sutured, leaving glass and gauze drainage in the pelvis. The cyst was aspirated of 500 c.c. of an oily, yellow fluid and its edges sutured to the aponeurosis and peritoneum, and the cavity of the cyst drained with gauze and a rubber tube.

The patient made an uninterrupted recovery, but the fistula from the cyst was not closed. An examination of the fluid aspirated found it to be oily, thick, and yellowish in appearance. On standing it separated into two layers—the upper yellow and curdy, the lower greenish-brown and thinner.

Microscopically, cholesterin crystals and a few epithelial and blood cells and an unrecognizable, colloid-like material. Specific gravity, 1023. Much albumin, but no sugar. Neutral or slightly acid in reaction. No methæmoglobin. Cultures on bouillon and agar showed negative results. Digests albumin without the presence of an acid.

Mrs. McC., aged fifty-eight years. Family and previous history negative. Has had nine children and five miscarriages. Menopause when fifty years of age. Thirty years ago, without any known cause or trauma, she noticed on awakening that she had a mass over the stomach and just below the left costal margin. This was not accompanied by pain or vomiting. It was about the size of a large orange. No jaundice at any time; no diarrhœa. The tumor has slowly increased in size, and is more apparent at present from loss of weight in the past two months. She has never had any discomfort from this tumor-mass, and suffers no dyspeptic symptoms.

On admission the patient is a stout woman, without any subjective symptoms. The lungs are clear and the spleen and liver dulness normal. Her abdomen is flaccid, and reveals the presence of a tumor extending from the umbilicus to the diaphragm, moving with respiration, slightly fluctuating, and can be slightly moved by the examining hand. It occupies the whole epigastric space, and is evidently a cyst in the lesser peritoneum (?). Urine is negative. Blood count shows absence of anæmia, but a marked eosinophilia of the leucocytes. Gastric analysis reveals a trace of lactic acid, a total acidity of 20 per cent., and the absence of free hydrochloric acid. Microscopically the Boas-Offler bacillus was present.

Operation was urgently advised, but was refused. She is still in good health at the present time, five months after discharge from the hospital.

Of the new-growths occurring in the pancreas, carcinoma is the most frequent. Sarcoma, adenoma, and lymphoma are rare, while in general miliary tuberculosis the pancreas is frequently involved. Syphilis, both congenital and acquired, interstitial and gummatous, has been seen, but it is rare.

The head of the organ is most commonly involved in carcinoma, and the disease may be primary, or, what is more frequent, secondary to

malignant disease of the surrounding structures, especially the stomach. Males are affected most frequently; from forty to sixty years is the usual age, and the most common variety is the scirrhous form.

The early symptoms are very vague and often lacking entirely. A gradual weakening of the muscles and a steady loss of weight, together with anorexia, a feeling of fulness after eating, and other symptoms of dyspepsia, will be noticed. This is succeeded very often by lancinating pains, becoming continuous, attacks of vomiting, and an ever-increasing jaundice, with enlargement of the gall-bladder. Glycosuria, fatty stools, or other evidence of retained pancreatic secretion may be present and aid in the diagnosis. Emaciation becomes extreme, and a tumor can be felt on palpation in the epigastrium, tender, hard, and scarcely movable. There is seldom any temperature, and ascites is frequently noticed. Death usually occurs within twelve months.

In instances where the common duct is not pressed upon, as in those cases where the malignant growth is confined to the body or tail, jaundice is absent and the symptoms atypical, and are like those of any other malignant growth.

Pressure on the portal vein and vena cava may cause thrombus and its usual sequelæ.

The differential diagnosis of this disease is exceedingly difficult in the early stages and rather easy in the late stages. The development of obstructive jaundice following dyspeptic attacks, with a distended gall-bladder and a rather increasing cachexia, are the most important signs, together with the effects upon the stools of the absence of the pancreatic secretion.

Two diseases—viz., common duct obstruction with a gallstone or chronic interstitial pancreatitis—must be diagnosed, because they are usually cured by a surgical operation, while malignant disease is nearly hopeless.

In the gallstone affection there is nearly always a history of previous colics, because the stone must have passed the cystic and traversed the common duct before impaction near the head of the pancreas. The gall-bladder is not distended, the rigidity of the right rectus is marked, the jaundice does not deepen until of a greenish hue, but alternately fades and disappears, often accompanied by intermittent pain, fever, and even rigors. There is less loss of weight, and the disease may drag on for years, though the longer the time that elapses between impaction of the stone and its removal the greater the risk of a carcinoma developing from the gallstone irritation.

In chronic pancreatitis the history of gallstone attacks and its association with dyspepsia must be elicited. The age of the simple affection is earlier, and there is more tenderness. The cachexia is very slight compared to that of carcinoma, and the jaundice is not so intense.

The treatment of malignant disease offers but little hope of cure. Robson records fourteen cases where the portion of the gland affected was removed, with ten deaths. The risk of injury to bloodvessels, together with shock, gangrene of the duodenum, and peritonitis, is great. The biliary stasis may be relieved by a cholecystostomy or a cholecystenterostomy.

The following case occurred last year at the German Hospital:

C. F. G., aged forty-three years. Family history negative. Has had dyspepsia and constipation for many years, and was in very poor health during early adult life. Six months before admission he suddenly became jaundiced, and without any pain. There was bile in the urine and clay-colored stools. Continued yellow, with a gradual loss of weight and strength, until three weeks ago, when he suffered from severe pain in the gall-bladder region and radiating to the right shoulder and back; had hæmaturia also. This pain has continued and increased in severity.

Examination on admission reveals marked jaundice, emaciation, and a mass between the umbilicus and the right costal arch. There is anæmia and 11,500 leucocytes. The patient insisting upon an exploratory operation, despite the diagnosis of malignancy, the abdomen was opened and a carcinoma at the head of the pancreas found. The gall-bladder, which was very much distended, was aspirated and closed with Lembert suture. The abdomen was closed with silk tier sutures.

The patient never stopped oozing after operation. Transfusion was performed, and the wound in the arm also continued to bleed. Death occurred in twenty-four hours. No autopsy was allowed.

The technique of operations upon the pancreas will vary with the needs of the individual case. The organ may be reached: (1) Through the gastrohepatic omentum, above the stomach; (2) through the gastrocolic omentum, below the stomach; (3) through the transverse mesocolon, back of the colon and stomach; (4) from the loin, behind the peritoneum.

Extensive lacerations or wounds of the pancreas should be treated as early as possible after the receipt of the injury, and the wound sought and closed with suture, avoiding puncture of the main duct. All hemorrhage, of course, is controlled; but in cases where the blood-supply is greatly destroyed necrosis is likely to result.

The pancreas is reached by widely opening the lesser peritoneum and turning the stomach up; the organ can then be seen and palpated, and, if necessary, the transverse mesocolon may also be incised to directly reach the gland. It is best to drain after operations upon the pancreas, and to favor the formation of a pancreatic fistula rather than allow the retention of the digesting secretion.

In acute pancreatitis surgical intervention had better be postponed until the primary acute symptoms, with the accompanying shock, have abated, or until the appearance of symptoms indicating suppuration.

The treatment has been outlined early in this paper. Should surgical intervention be demanded an incision may be made above the umbilicus and about four inches long. After opening the peritoneum the omentum may be examined for fat necrosis, and a vertical incision made in the gastrocolic omentum, opening the lesser sac. The pancreas can then be examined, and an incision in the transverse mesocolon will expose the gland and confirm the diagnosis. A second oblique incision is then made in the left loin at the costovertebral angle, and the lesser peritoneal sac cleansed of blood and packed with gauze. Partial suturing completes the operation. Prompt stimulation must be used to combat shock.

Chronic pancreatitis must be treated by abdominal section and cholecystostomy. The operation of cholecystenterostomy and choledochoduodenostomy are harder to perform and are not as effectual in securing free drainage.

Cholecystostomy. The gall-bladder is exposed by an incision through the right rectus muscle, and excepting in highly infectious cases is generally freed from adhesions, which when met with usually involve the abdominal wall, liver, omentum, duodenum, pylorus, and colon. The gall-bladder is isolated by gauze pads and aspirated of its contents. The puncture is then enlarged and the gall-bladder examined for stones; if present they may be removed with forceps or scoop. A small piece of iodoform gauze is introduced into the gall-bladder and the opening temporarily closed with hæmostatic forceps; the gall-bladder is then brought into the wound, if possible. A piece of gauze is passed around the gall-bladder in such a manner as to allow the lower end of the gauze to protrude from the lower end of the wound, and the gall-bladder is sutured to the aponeurotic layer of the abdominal wall. Before tying the gall-bladder sutures the gauze pads are removed, but not the gauze around the gall-bladder. The sutures are tied, the wound above and below the gall-bladder closed, the hæmostatic forceps removed, the piece of iodoform gauze taken out of the gall-bladder, and a solid rubber drainage-tube carried into the gall-bladder. This drains into a receptacle at the side of the patient.

The results of surgical treatment in this class of cases is very encouraging. Of twenty-four cases operated upon by Mayo Robson, in twenty-one a complete and perfect recovery ensued.

The operative procedure in pancreatic cysts will depend upon the degree of adhesion to surrounding structures; and as this almost invariably occurs, the extirpation of the cyst is difficult unless, as is the case in rare instances, the cyst is pedunculated. Aspiration of the cyst should only be performed when the patient is severely ill from diabetes or the effects of pressure. The cyst will always refill, and the danger of leakage into the peritoneum from the point of puncture is very great.

Whenever practicable the abdomen should be opened by a median incision above the umbilicus and by incising the gastrocolic omentum. This exposes the cyst. Its contents should be withdrawn by an aspirator, as the needle is removed closing the puncture with one or more hæmostats. The cyst wall is then drawn to the wound, and the subsequent procedures are exactly as in cholecystostomy, viz., suture of the cyst wall to the parietal peritoneum and draining the cyst. Where some of the contents of the cyst escape during aspiration it is safer to make a second incision in the loin and drain the lesser sac. Körte collected eighty-four cases operated upon by this method, with five deaths.

When the cyst is small, and from its position and relations cannot be brought to the abdominal wound, the rubber drainage-tube should be introduced into the cavity of the cyst, and by careful gauze packing so surrounded that leakage is prevented.

Malignant disease of the pancreas is better left alone, or a palliative measure performed, such as cholecystostomy or cholecystenterostomy.

X-ray Findings in Pathological Conditions of the Pancreas.

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It will generally be admitted that the X-rays may ultimately play a very important part as an aid in recognizing pathological conditions of the abdominal organs. Even at the present time much valuable collateral information may be obtained from this source, providing the picture as seen on the fluorescent screen or the photographic plate be properly interpreted.

While it is true that too much reliance should not be placed in the findings of the X-ray laboratory, especially in cases that involve the abdominal viscera, it is equally true that any possible errors are entirely due to the personal equation of the operator. It is probable, therefore, that as operators, with increased experience, improve their technique or have access to improved tubes and other pieces of apparatus, this source of error will be largely if not entirely eliminated.

The possible causes of errors of this kind become more evident when we remember that conditions of any kind manifest themselves, under the X-rays, as what are popularly termed shadows, and that these shadows, in turn, are caused by relatively dense masses of matter which intercept or absorb the rays of energy emanating from a vacuum tube. It will readily be appreciated, therefore, that in the abdominal cavity we may have causes for a variety of shadows of different densities, and that these shadows may or may not be due to pathological changes.

If we bear in mind, then, that X-ray findings, at the present time at least, can hardly be considered to furnish more than corroborative

evidence, we will not be likely to be carried way with the success or failure of a few isolated observations.

Among the organs in the abdomen the pancreas would appear to offer a most promising field for observation and study by means of the X-rays. Under supposedly normal conditions the head of the pancreas shows but a faint shadow on the photographic plate or the fluorescent screen; and while it is true that there are abnormal conditions, not necessarily pathological, that will increase this shadow to a considerable extent, these can, in many cases at least, be differentiated from the comparatively dense shadow that is always produced by an enlarged or hypertrophied pancreas.

With a view of soliciting comment or criticism, and also with a view of inducing others to follow or improve on our technique, it may be well to give an outline of our methods of procedure.

For the study of gross pathological conditions we have found the fluorescent screen to be more satisfactory than the photographic plate. It should, however, be understood that this applies solely to the gross examination and not to definite determinations of the presence or absence of any more minute details, such as a fracture of a rib or a renal or ureteral calculus.

The apparatus used for generating the X-rays is the ordinary type of induction coil, giving approximately a ten-inch spark. The tube that is usually preferred is one of the self-adjusting type, with extra heavy anodes, so as to take a considerable current without risk of destroying or puncturing the platinum plate. For examining patients we use a wooden table with heavy rollers and a comparatively thin wooden top. This table is so arranged that the vacuum tube may be placed under the patient and the latter moved at will to any position over the tube. In this way we are enabled to make a rapid and satisfactory survey of the different portions of the body without running any risk of either the patient or the operator coming in contact with the tube or the lead wires attached to it.

This method of examining has several advantages. In addition to the patient being perfectly safe from the electric current, he is comparatively comfortable, being perfectly at rest and always at the same relative distance from the anode of the tube. In addition to this, the light from the tube may be readily screened, so as not to interfere with or blur the image on the fluorescent screen.

The facility with which a complete survey of the whole body can be made is of importance in that it permits of a comparative study of the structure and muscular development of each individual. The uses of this will be recognized when we remember that each individual is a unit to himself as to structure or development, and that any undue muscular development may and often does cause shadows that may be misleading.

Having taken this preliminary survey, and satisfied ourselves of the absence of other possible pathological conditions, we will usually find, in cases of congested or hypertrophied pancreas, a distinct and comparatively dense shadow extending a little to the right of the median line and about midway between the lower end of the sternum and the umbilicus. In the majority of cases the shadow will be found to be rather longer than wide, and it seldom extends to the left of the shadow cast by the spinal column. One distinctive feature of the shadow cast by the pancreas is the fact that it is not readily movable with the motion of the diaphragm. By this simple characteristic we are usually able to differentiate between an enlarged or dense head of the pancreas and any pathological change involving the liver or stomach. Here, again, it must be borne in mind that we may have inflammatory conditions involving either of these organs that will produce adhesions, and these in turn will inhibit, or at least restrict, the natural range of motion. As a rule, however, such adhesions will also restrict, to a considerable extent at least, the normal range of motion of the diaphragm.

Another distinctive feature may be established by taking advantage of the fact that the pancreas is located near the posterior wall of the abdomen, and on this account the resulting shadow is readily displaced by changing the relative position of the body, tube, and fluorescent screen. For instance, if we move the cause of the shadow above the anode of the tube the shadow is thrown high up, but when moved in the opposite direction it appears to be comparatively lower down.

On a photographic plate the shadow is usually best shown from the posterior aspect. The plate should be placed against the back and extend from about the ninth dorsal to the fifth lumbar vertebra, with the anode of the tube about the median line and midway between the lower end of the sternum and the umbilicus.

Among other conditions that give abnormal shadows in this region we may have an undue overlapping of the kidney and the head of the pancreas, a floating right kidney, or even an enlarged or cystic kidney, though the latter may usually be recognized, being much larger and more sharply defined in outline.

A few of the objects that are particularly to be guarded against may be mentioned here. They are, among others, masses of food or even water in the gastro-intestinal tract; and for this reason it is preferable to make the examination, as nearly as we can, when the stomach and small intestines are comparatively empty.

Undue or uneven layers of clothing should be avoided. This is especially true of garments made from fabrics dyed black, as the latter are usually mordanted with either iron or chromium salts, and will usually give distinct and sometimes very dense shadows on the fluorescent screen or photographic plate.

Observing these few simple precautions, and always bearing in mind the possible differences in density of shadows due to the varying thickness or development of the several patients, we are not likely to go far astray in locating an abnormal or particularly dense shadow. The cause of the shadow must, of course, be more often determined from the clinical data than from the location or size of the shadow as determined by means of the X-rays.

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TROPICAL ABSCESS OF THE LIVER, WITH REPORT OF A CASE.

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The patient, Max G., aged thirty years, a native of Russia, applied at Medical Clinic No. 1, of the Philadelphia Polyclinic, on September 2, 1901, and in Dr. Cohen's absence from the city was seen by Dr.

Truman Augé, chief of clinic, from whose excellent notes much of the history that follows is taken:

History. Three years ago, while in South Africa, being shut up in Kimberly, with insufficient food and bad water, the patient suffered an attack of illness characterized by looseness of the bowels, the stools occurring ten to fifteen times a day, being dark in color and streaked with blood or containing bright blood. The stools were not accompanied by pain. The patient's appetite remained good. The stools had not a particularly offensive odor. No record of fever could be obtained. His feet were swollen, and he lost flesh and strength. The intestinal discharges were at times apparently normal, but after a brief period would return to their former condition. Two months after the onset the illness was diagnosed dysentery by the physician then consulted; the patient suffered intermittently for about eighteen months, when he determined to leave South Africa. His condition improved as soon as he got on board ship. During the voyage he gained flesh and felt better, but did not gain in strength. The voyage lasted twenty-eight days. Improvement continued for about eight months after landing in this country. The swelling of the feet disappeared entirely two months after leaving the ship. About a year before his visit to the Polyclinic the bloody stools recurred, and had, according to the patient's statement, continued intermittently ever since. There had not been chill or fever. The patient attended the dispensary irregularly for about a month, during which time the condition of the bowels improved. Dr. Cohen saw him on October 7, 1901.

Physical Examination, October 7, 1901. The heart was displaced to the left and upward, the apex-beat being felt in the fourth interspace and nipple line, but otherwise normal. The sounds were weak; the pulse feeble but rhythmical, and not very rapid. The exact rate was not recorded. No pulmonary lesion was found. Both lungs were compressed, the right more so than the left. There was no effusion. On examination of the abdomen a mass was found occupying the right hypochondriac and umbilical regions. Its percussion-note was continuous with the normal liver dulness, which was also much enlarged upward, beginning in the fourth interspace at the right border of the sternum but in the mid-axillary line at the upper border of the fifth rib. The mass had a mean projection of one and one-half inches. It was tense, hard, and smooth; the lower edge was rounded and could be distinctly traced at a mean distance of about four finger-breadths below the ribs; the left border running from the apex of the heart to about one inch above the umbilicus, the margin then dropping to the umbilicus, and thence running to the right mid-axillary line at the same level on a curved line, with convexity outward. Posteriorly the dulness extended on the right of the spine from the ninth rib to below the costal border, reaching about three inches to the left side of the spine and tapering to a point. The splenic dulness began at the seventh rib in the paramammillary line, at the eighth rib in the posterior axillary line, and extended transversely from this point to the mid-scapular line, merging below with the dulness of the liver, these conditions probably indicating an enlargement as well as a displacement of the organ backward and upward. At the most prominent part of the mass, about an inch below the tip of the xiphoid cartilage, there was a circular area about as large as a silver dollar, having an elastic "cystic"

resistance. There was no pain or tenderness over the enlarged liver or over the abdomen and thorax at any point. Neither the thoracic nor the abdominal wall was reddened. There was no œdema. The abdomen outside of the dull area was tympanitic. No distinct hydatid tremor or fremitus could be found, but there was an indistinct and inconstant crepitus which could be heard over the tumor, and which it was thought might be due to daughter cysts rubbing against one another. The superficial veins of the abdomen were but slightly distended, and, except in the right groin, no lymphatic enlargements could be detected. A number of white scars were seen over the right hypochondrium and right chest, which the patient attributed to "winter pox" occurring in his childhood in Russia. The patient denied any venereal disease. The enlargement of the abdomen was first noticed aboard ship, shortly after leaving Africa, and it seemed to increase before an attack of dysentery and diminish afterward. It had given him no inconvenience, nor would he have thought it worth mentioning if examination had not been made. The patient was not jaundiced and not apparently anæmic. The tongue was but slightly coated. The blood, feces, and urine were examined by Dr. Coates, of the Polyclinic Laboratory, with the following findings:

Blood. Hæmoglobin, 80 per cent.; red blood cells, 4,570,000; leucocytes, 13,400—no abnormal bodies. Feces: bacilli coli communis; staphylococci; no amœbæ. Urine: amorphous urates; uric acid crystals; a few granular casts. Reaction strongly acid. No parasitic ova. No sugar; no albumin. Sulphates normal. Chlorides, 1 per cent. Urea, 3.2 per cent. Indican, small amount. No leucin or tyrosin; bile pigment and biliary acids absent.

Diagnosis apparently lay between abscess of the liver of amœbic origin and hydatid cyst. The long duration of the tumor, its enormous size, and the absence of the usual symptoms of abscess were strongly in favor of hydatid cyst; the history of the dysentery, however, which originated in South Africa, caused us to consider strongly the question of amœbic abscess. The patient had suffered no pain excepting recently, and that of only a transient kind. There was no tenderness and no history of previous tenderness. The elevation of the temperature was insignificant, and there was no history of marked fever or rigor at any time. The patient's general health was apparently good. The blood showed no marked leucocytosis. The amœbæ were not found after repeated examinations. There was no œdema over the liver, either in the thoracic or abdominal wall. The character of the enlargement, its smoothness, the absence of tenderness, and a sense of fluctuation at its most prominent part also tended to confirm the idea of hydatid disease. Strongly in favor of abscess was the fact that the patient reported that an exploring needle had been introduced into the swelling and that pus had been withdrawn; as this exploration had been made by a competent physician we were obliged to attach to it considerable importance. At the same time, however, it must be remembered that fluid similar to that described by the patient might have been obtained from a suppurating hydatid cyst.

The operation was performed on November 6, 1901. As the tumor involved the anterior portion of the liver more extensively than the posterior, it was determined to approach it through an incision just below the very much elevated costal border. A straight incision

three inches in length was made over the most prominent part of the tumor. The peritoneum was not adherent, and there was no fluid in the abdominal cavity. The liver appeared somewhat darker than normal, extended nearly down to the right iliac fossa, and on its upper surface, which was moderately adherent to the diaphragm, gave a sense of distinct fluctuation. An aspirating needle was introduced into the liver, and through it flowed a thick, brown pus. The general abdominal cavity was thoroughly walled off from the point of puncture by large gauze pads. After the withdrawal of the aspirating needle the abscess cavity was freely opened by means of the Paquelin cautery. An enormous quantity of pus of the character above mentioned escaped through a glass drainage-tube which was introduced, but, unfortunately, the exact amount could not be ascertained, because of the necessity of constant irrigation in order to prevent infection of the general peritoneal cavity and in order to thoroughly cleanse the abscess cavity; certainly, several quarts of pus were removed. When the abscess cavity had been emptied the liver had so contracted that the opening made by the cautery was no longer opposite the abdominal incision; therefore, a transverse incision was made along the costal border at right angles to the primary incision, a rubber drainage-tube and the packing being brought out of the lower end of this second incision. The patient reacted well from the operation.

There is very little to report in the subsequent clinical history of the case. The patient suffered from some cough for a few days after the operation, but otherwise made a very satisfactory recovery without complication. The drainage was at first profuse, but gradually diminished until about the middle of February, when it entirely ceased. Two points are worthy of note in the post-operative history: a very great increase in weight and a rapid contraction of the liver. An examination of the pus showed it to be sterile, and no amœbæ were found. Repeated examination of the pus and detritus failed to demonstrate the presence of amœbæ.

Pathology. The frequency of liver abscess among our soldiers in the Philippines and among the British in South Africa has brought this question into considerable prominence in English literature. Robinson[1] says that in 96 autopsies done on soldiers dying from dysentery in the Philippines liver abscess was found twelve times. Of course, pyæmia, traumatism, gallstones, and roundworms frequently produce abscess of the liver, but probably the most frequent cause of single abscess is some form of dysentery. And further, the amœbic type is that which most often produces the condition. The amœbæ can often be demonstrated in the scrapings from the abscess wall when not to be found in the pus itself. It is to be regretted that in this case the wall of the abscess was not scraped with this object in view. Although we look upon multiple abscess of the liver as usually of pyæmic origin, yet the fact that about one-half of the liver abscesses occurring in tropical countries are multiple would incline one to the view that

[1] Journal of the American Medical Association, May 12, 1900.

the amœba is more frequently than we suppose the cause of this variety. Giordano, of Venice, in discussing this question before the Intercolonial Congress of Medicine, 1900,[1] said that alcoholism was often a great predisposing cause of liver abscess, and in this view Adami agreed, though he asserted that the determining cause was an ascending angiocholitis of intestinal origin. These statements regarding the predisposing tendency of alcohol may explain, to some extent at least, the greater frequency of liver abscess among American soldiers in the tropics than among the more temperate natives. The abscess may be found at any point in the liver, but is most frequently situated in the right lobe either near the anterior or posterior border. If left to itself the abscess will, in most instances, rupture into the pleura or lung, although rupture into the peritoneum or on the surface is not rare. Spontaneous cure often results from rupture into the lung, as in the case recently reported before the County Medical Society by Dr. Boston, but, of course, to wait for such an occurrence would be extremely unwise and comparable to the fallacy of waiting for adhesions to form after making a diagnosis of appendicitis. It is needless to say that unless immediate operation is done intraperitoneal rupture is invariably fatal. The mortality of liver abscess without operation is between 90 per cent. and 95 per cent., those cases recovering usually doing so after rupture into the lung.

Treatment. The treatment, when once a diagnosis is made, is entirely surgical, and consists in thorough opening and thorough drainage. The aspirating needle may be looked upon in some instances as a safe diagnostic means when proper aseptic precautions are taken, but it is by no means a sure measure, and should only be employed when the surgeon is prepared to proceed at once to operate in case pus is found. This is particularly true when the abscess is situated anteriorly, for here the infected needle must traverse the peritoneal cavity, which is in most instances not shut off by adhesions. It is quite true that in many cases the needle is used, pus is found, immediate operation is not done, and the peritoneum is not infected; in fact, it was true in the case here reported; but the practice is a bad one, exposing the patient to considerable unnecessary risk. Anyone having experience with the exploring needle needs not to be told of its inaccuracies or how very misleading its evidence oftentimes is. The proper time for the employment of this instrument arrives when the liver has been exposed by a free incision and the surrounding cavity, pleural or peritoneal, properly protected with gauze. At this stage the needle not only locates the abscess but indicates to the operator the best point at which to drain. There are two recognized methods of operating in

[1] British Medical Journal, October 13, 1900.

this condition, and between them, foreign surgeons particularly, are much divided. The first operation is that of immediate drainage, while the second consists in exposing the liver, allowing it to become adherent to the abdominal wall, and then opening it twenty-four or forty-eight hours later. In the hands of an experienced surgeon the former operation would certainly seem to be the most satisfactory procedure. Under doubtful aseptic circumstances an inexperienced operator would probably be wise to follow the second method. Smits[1] reports, from the island of Batavia, the most gratifying results from the employment of the two-stage operation, 16 recoveries out of 19 operations. It is doubted, however, that these good results were altogether due to the two-stage operation. After the location of the pus by the needle we believe that there is no better instrument for incising the liver tissue over the abscess than the Paquelin cautery. Curettement of the abscess wall is a measure strongly advocated by Fontan, but its employment in abscesses of short duration would seem questionable and, in fact, the present case would tend to show that it is not an essential part of the treatment even in abscesses of long duration. In the introduction of the drainage-tube care must be taken that the end of the tube does not rest on the abscess wall, else such pressure might produce necrosis and perforation at this point. One point in the technique of this operation which is frequently dwelt upon is the stitching of the liver to the abdominal wall. This procedure does not seem necessary if the precaution is taken to carefully surround the tube with gauze, and might possibly interfere with the subsequent contraction of the abscess cavity. It was not done in the present case nor in another recently seen in which an equally good result was obtained.

A STUDY OF SOME CIRRHOSES OF THE LIVER.

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No doubt the majority of practitioners believe they know pretty well about cirrhosis of the liver. It is a common affection, particularly in hospitals and dispensaries. In its advanced stages it is readily diagnosed, as a rule.

In regard to its prognosis and treatment: These appear relatively simple in that formerly at least it was assumed by very many that we had to do with a fatal complaint; and as for remedial measures, they resolved themselves into few, among which paracentesis at the last

[1] New York Medical Journal, February 9, 1901.

stage only was imperative, mainly to relieve distress. How far such notions to-day are removed from truth I shall endeavor to show later.

That the liver is a difficult organ to study and know accurately few will deny whose opportunities and mental make-up prove them competent observers. As compared with other abdominal or thoracic organs, where does it stand? The lungs can be inspected, palpated, percussed, auscultated, and in a way measured. So, perhaps, can the liver; but in the former case we seem to be in more accurate touch latterly by reason of sputa examinations under the microscope and inoculation experiments. The heart and its disorders have been the source of so many investigations in the physiological laboratory, so many accurate clinical observations in the office and the class room, hospitals, and dispensaries—everywhere and at all times—that little new may be added. With the advent of physiological chemistry, the use of the microscope, and the opportunity, daily or hourly almost, of knowing precisely what the urine shows, the kidneys as organs are very clear to us. With the liver, on the contrary, much seems still conjecture and hypothesis. We speak of its torpidity, engorgement, anæmia, its functional derangements, its organic lesions, with glibness at times; and yet there is much that is obscure about its functions, healthy and morbid, that is by no means evident, and about which there are very honest and almost irreconcilable differences.

In this connection, only very lately, Dr. Goodhart writes: "The largest organ of the body, its imports and exports must be enormous, and from the familiar way in which it is spoken of there cannot be a man in the whole world who does not think he knows all about it. But what are the facts? We know something about the physiology of the liver; but this knowledge has been mostly obtained by experimentation on the lower animals, by observations that occasional cases of disease afford us, and by certain inferences that we draw—very much at second hand—from the changes produced by disease in the organ. But all these things—valuable as they are, and without which where we should be I do not know—yet are very far from giving us that real and intimate knowledge of the living organ that we require to enable us to treat its diseases."[1]

Should this not be adequate reason why we approach the study of the cirrhoses with much diffidence and full recognition of our deficiencies, even in the rôle of an upright reporter? "Good men and true" have essayed this work faithfully in the past, and told us many things we should know. A great deal more is required, much research remains to be done, and only by degrees may we legitimately hope to secure truth—entire and with full details.

[1] British Medical Journal, August 3, 1901, p. 251.

In what relates to the cirrhoses there are many undetermined questions. The views ordinarily held are not entirely correct. In the first place, the clinical facts, the more we become conversant with them, do not justify invariably the gloomy prognosis of these affections which has been entertained. Instead of separating with discrimination, there has been confusion, because all forms of the disease have been thrown together and included as one. In fact, here as elsewhere, the work of the dead-house has reigned supreme for a time, and the close watching of patients during life has been deemed of lesser value, when it should always, as I believe, be the first thought of every good physician. How, indeed, can we treat a patient properly unless we know just what symptoms he presents during life and in what manner and to what degree function was disturbed? Everyone who has grown gray in harness and whose experience has widened and deepened knows that the morgue and the laboratory by themselves ignore too much and too often the intricate and obscure of our economy in a dynamic sense, and hence must be always controlled, as it were, from the horse-sense point of view of even the humbler humdrum daily worker at the bedside.[1]

There are different forms and degrees of cirrhosis. Not all at once and every time does the final atrophic stage, with its irremediable anatomical conditions and its absolutely gloomy horoscope, show itself. This form is slow and insidious of development. At first it is not recognized; there are few or no symptoms we can attach to it. At best we can only be suspicious.[2] If we have to do with a chronically hard drinker of beer or spirits, of course, we think of the liver and fibroid changes; and then if there be palpitations of the heart, evidences of dyspepsia, vascular stigmata on the face, corpulency, and a somewhat enlarged liver we cry a halt to bad habits, and the outlook may be sombre. On the same lines, if we find loss of strength, inappetence, and a failure of nutrition, as shown by loss of weight, even though the liver be of normal size apparently, we cannot avoid somewhat gloomy forebodings unless we are able soon to control habits and regimen. But are we sure—may we be reasonably certain—with such vague characters that we shall even later be able to fix an absolute and correct diagnosis? The answer—the only one—must be negative. The sooner the better for every medical student to know that disease does not run closely at any time along so-called prescribed lines. It varies, it differs; one day we see certain forms of disease, another day it is just the contrary. All cases are in a certain sense individual,

[1] Vide Andrew Clark, British Medical Journal, February 3, 1883, p. 191: "Address on Clinical Investigation before the Clinical Society of London."

[2] In writing of early stages of hepatic cirrhosis, Billings claims there is a relatively large number of patients whose symptoms are those of neurasthenia, myalgia, mononeuritis, or gastro-intestinal disturbance.—Medical News, July 26, 1902, p. 167.

personal. There is nothing wholly general and all-absorbing about any one instance. Take, for example, the abdominal effusion in cirrhosis—the ascites which in the later stages is so striking, so characteristic, so grave of import in the eyes of many that it seems like to a funeral knell in its fatality. Is it so? May it not appear soon, and in its earlier stages may it not be treated wisely and advantageously? And may not a patient do well for a long while, thus treated? And why is this? May not very many of the liver cells still be functionally healthy, quite capable of carrying on good nutrition? Is not fibrous growth in the liver usually slow? Does it not leave many lobules untouched for many a day by its contracting power, and otherwise in what degree is it really pernicious? These and other queries immediately arise to one's mind. It is, moreover, a fact of daily experience almost to have patients come to our office or to out-door clinics in whom ascites is undetermined. We are unable to affirm positively that it exists. And this is true not for one examination only, but for many. Days, months, and even years elapse with some patients before we can say convincedly this *is* or this is *not* a case of hepatic cirrhosis.

The three principal forms of cirrhosis which are recognized by writers are (1) atrophic, (2) hypertrophic, (3) syphilitic. Besides these there are so-called minor, even undetermined, forms. Usually the latter are due to passive congestion, brought on by pressure from neighboring tumors or indicative of some chronic disturbance of heart power, structure, or action. In these instances, especially where the heart is the primary cause, the abdominal ascites is merely a symptom which is part of a general anasarca. It may be, however, that the ascites has something special in it; it may stand by itself, as it were, so far as effusion is concerned in the serous cavities. Then we have to do with an expression of cardiac inefficiency accompanied by one of the known effects of portal obstruction due to fibrosis around the vessels of the liver. In these cases we should look rather for hypertrophy than atrophy. The liver is enlarged and engorged. It is filled with blood from overcongestion. There may or may not be already marked fatty change, and thus, instead of the dense, hard, tough liver with sharp lower margin, which is said to characterize the cirrhotic liver, we may have a greasy, rather soft structure, which leaves the impress of the finger upon its surface when we press with even very moderate force. While, then, it may be admitted, and is certainly true with limitations, that all three forms of cirrhosis of the liver are characterized by increase of fibrous tissue, which penetrates its structure and distributes in somewhat different ways along the branches of the interstitial tree, it is also true that these forms are all different in many particulars.

Their pathology, to begin with, is not the same. In one form—the hypertrophic—the fibrous tissue is finer, less formed, accompanied by

a cellular growth, and runs along the smaller branches interstitially. In the atrophic form this fibrous tissue is coarser, better formed, shows greater tendency to contract upon and disorganize liver cells, extends along larger branches of the interstitial tree, and is not accompanied by cellular growth to the same degree at all.

In connection with the increase of connective tissue it has been proven experimentally that the action of alcohol on the liver of animals is also to cause granular and fatty degeneration of the liver cells. According to Vaughan, the increase of the connective tissue is small in amount, and only reported by some observers. Vaughan concludes that " the connective tissue changes are subsequent to and dependent upon alteration in the hepatic cells."[1] Later on he writes that with the clinical and experimental evidence hitherto obtained we are justified in believing " that in alcoholic cirrhosis the pathological changes begin in the hepatic cells."

From what has been said concerning the pathology and etiology of atrophic and hypertrophic cirrhosis it has been shown that the two forms may exist as types. They may also be present combined, as it were, in the same individual and exist as one disease. The atrophic form is clearly due, as a rule, to alcohol; the hypertrophic to infection (Vaughan); but the infection may precede or follow the toxic poisoning, and the result is a mixed form of cirrhosis. These forms, both clinically and at the autopsy, are very difficult of precise diagnosis, so intimately and curiously combined are their symptoms or lesions.[2]

In the syphilitic cirrhosis we have those broad bands of fibrous tissue which penetrate between the lobules and draw the liver down near the surface in such manner as to leave the puckered, scarred appearance, with bossy, prominent, irregular masses between which are so characteristic.

As to the course and clinical symptoms: These, we shall see, differ widely and obviously in many ways. In atrophic cirrhosis, for example, the main distinguishing clinical feature, as we could almost premise from its pathology, is the evidence of marked portal obstruction—at least this is true almost as soon as the disease is clearly determined. Hence arises the abdominal effusion, and with this most significant and almost portentous sign we have hemorrhages from the stomach and bowels. Sometimes these are small and infrequent, and give no great and immediate alarm if their quantity alone is consid-

[1] Journal of American Medical Association, October 5, 1901, pp. 878, 879.

[2] In a patient I saw last summer, who subsequently died, the liver was stated during life to be *much enlarged* by several very competent observers—both surgeons and physicians. I was able to satisfy myself after death, by intra-abdominal digital exploration, that the liver was *not notably* enlarged. I was also convinced that an intra-abdominal mass, in close juxtaposition with the lower margin of the liver, gave rise to an error of diagnosis in this regard, although the case was proven not to be one of cirrhosis of the liver.

ered ; but considered from the point of view of their evident causation, great apprehension is invariably excited, and justly so. Shortly we may have, and do often, those abundant and depressing blood losses so difficult to arrest, and which point to the urgent necessity, and none too soon, of employing all rationally known measures to ease up an obviously crippled organ and to restore falling strength. How unfortunate it is in such cases if the somewhat too enthusiastic surgeon finds indications for abdominal exploration or an operation for internal hemorrhoids! Jaundice is a rare sign in these cases[1]—at least real jaundice, with urine loaded with bile pigment and acholic stools. Of course, the dull, earthy hue of the skin and the subicteric tint of the sclerotics are frequent phenomena which serve in a measure to fix our diagnosis. Sometimes " adhesive pyelophlebitis closely resembles the atrophic form of interstitial hepatitis. The rapidity with which the peritoneal effusion reforms after tapping is an important diagnostic sign."[2]

These cases of atrophic cirrhosis in reality are long as to duration. They appear short merely because they are unrecognized prior to the advent of the ascites, and then the inevitably fatal termination seems to stand out imminently, since a few months or a briefer period may bring about a fatal ending of the case.

The first and imperative thing to do with these patients is to lay down the law which forbids alcoholic stimulation in any form, because, as we know, in the chronic irritation thus produced we find the immediate and efficient cause of the majority of such cases. Of course, there are degrees of injurious action. The man who has drunk heavy beers for a long while and in large quantities, combined, it may be at times, with daily potations of spirits undiluted and containing fusel oil, is the worst type with which we have to do. Such an one is the longshoreman, hodcarrier, and other laboring man, or the chronic loafer who comes to our out-door clinics or to our hospital ward, when, on investigation, we find the contracted, small hobnailed liver, which shows the condition of multilobular cirrhosis and also many accompanying pathological changes. The spleen and pancreas are often hard and functionally decrepit, the kidneys show marked interstitial changes, the stomach is thickened, atrophied, and congested ; but, above all, the heart is weak, flabby, degenerated. Fibrous myocarditis is sometimes made out at the autopsy ; more frequently we have more or less fatty change, apparent to the eye and corroborated with the microscope. The general vascular system does not escape, and capillary

[1] Where fatty degeneration and cirrhosis coexist profound, persistent jaundice is less infrequent. A patient thus affected, as shown by the autopsy, died in one of my wards at St. Luke's Hospital May 8, 1902.

[2] James H. Wilson, Medical Record, December 7, 1901, p. 909.

arteriofibrosis has run its course, so that there is scarcely a sound arterial coat to be found, no matter what organ we turn to. This is, indeed, a gloomy and, alas! too true a picture. Alongside, fortunately, we have another far more hopeful. The man-about-town, the broker, the business man—even the lawyer and the not too wise physician—whose drinking consists in two or three or more "Manhattan" or "Martigny" cocktails every day, taken upon an empty stomach and as "a pick-me-up," as the saying goes; the genial, pleasant fellow who gives himself a rest of an evening, and who frequents the club and the billiard-room, and who before the evening is gone has consumed several drinks of "rye" or "Scotch" or "unsweetened," is also an apt candidate for admission among the cirrhoses of the atrophic order. Fortunately, such an one drinks good spirits, as a rule, in the sense that it is relatively pure and unadulterated. Moreover, his food is well cooked and assimilable. He bathes, and is therefore cleanly and has an active skin; and with a healthier body, perhaps, to start with he does not suffer so soon or so hopelessly as the poor chap I have previously considered. Moreover, when the first premonitory signs of disease occur, if he be even moderately wise, he consults his family physician, when I would fain believe he secures a mental and moral shaking up, with which a little useful medicine added thereto allows him to guard more carefully his still useful liver cells, and gives declared fibrosis an opportunity to cease development and extension for a time.

Without going further in this description I trust I have been able to show and bring home to my readers what they all know, what they all feel and see around them every day. Turn, now, to our hypertrophic form of cirrhosis, and what may we note? Here, instead of atrophy and contracture and loss of size, we have enlargement and increase of weight. In addition, there is to be found a singular development of new biliary canaliculi on the periphery of the lobules, which is so distinctly shown in sections for microscopic insight. This latter division is the one so ably described by Hanot, Charcot, and other French writers, and about which there is such wide divergence of opinion elsewhere. Suffice it to add that in typical forms these must be very rare, infrequent cases. For my own part, I do not recall to have seen and observed a typical one—at all events, not one where the post-mortem researches justified altogether a previous clinical diagnosis. In the hypertrophic cirrhosis of the sort we do see from time to time the fibrosis as it extends into the liver seems to mark for its own a few cells here and there throughout the structure, or certain individual lobules. In this hypertrophic form ascites does not often occur, nor should we expect it if we pay due regard to the special characters of the fibrosis formation. Jaundice, on the contrary, is a marked and almost omnipresent symptom; and it is the real jaundice—not the

aborted state, so to speak—to which I have referred in the atrophic form of cirrhosis, *i. e.*, icteroid hue.

Like to atrophic cirrhosis, hæmatemesis is not infrequent, and, when it occurs, abundant and very threatening. Many of these hemorrhages in cirrhosis originate at the lower end of the œsophagus. They are often confounded with hemorrhages which come from ulcer of the stomach.[1] In either case, but especially the former, we should be very chary about the introduction of a stomach-tube, as a dangerous or even fatal loss of blood might take place immediately. With the hemorrhage from the œsophagus or stomach we see developed many acute symptoms. There is fever, and often the temperature ranges high. There is delirium of an active kind, pointing to a toxæmia and blood infection. "Chills and sweating are not common" in the hypertrophic form of interstitial hepatitis, "thus serving to differentiate it from impacted gallstones." (Wilson.)

Later the patient may relapse into coma from which there is no awakening. Before these symptoms of delirium and coma become manifest we usually have several repeated intermittent attacks of pain, with fever. The pain is localized over the hypochondrium, and the liver is tender.

In these particulars we have an approach to the syphilitic form, and except for the history, the different physical signs, and other symptoms, we might have a difficult diagnosis; but this is not true for the careful diagnostician, who also considers the ordinarily chronic course of the disease.

As to causation, it is obscure. Frequently the spleen also being enlarged a malarial origin is suspected. There are too few observations accurately made in which the plasmodium has been discovered to altogether justify this opinion. I rather believe that alcohol is here again a more probable and efficient factor in bringing on this change in liver structure. One statement would seem to be borne out by facts that we do know, and it is that the obstruction of the bile ducts by fibrous tissue seems to account for the genesis of the acute symptoms which mark the course of the disease and point to inflammatory conditions, more or less lasting. According to some authors, such inflammatory conditions are wholly ignored, and they affirm that an infective process is the sole, undeniable cause of hypertrophic cir-

[1] According to Knapp (Medical Record, March 1, 1902, p. 334) these hemorrhages are sometimes erroneously "diagnosed as pulmonary tuberculosis," when they should be considered "cases of ulcer of the œsophagus."

According to Bouchard (Revue de Médecine, October, 1902) hemorrhages in cirrhosis, which occur outside the territory of the portal vein, are in relation with pre-existing arterial lesions, affecting various organs, and do not depend upon abdominal plethora. The arterial lesions are chronic degenerative changes probably due to arterio-sclerosis.—Boston Medical and Surgical Journal, September 11, 1902.

rhosis. In this conection Vaughan[1] writes: "With our present knowledge it must be attributed in all cases to infection." If this be admitted, pathologically, it may be stated that "the epithelium of the gall ducts is the site of the primary involvement." (Vaughan.)

In the syphilitic liver we find marked induration, at times fairly recognizable by our tactile sensations. The liver itself is, as a rule, larger than normal. This is not an invariable rule, and just the contrary may be found, no doubt, in those instances where the fibrous contracting bands are broad and numerous. The gummata on the surface of the liver when they exist are often easily recognizable. Of course, we may confound them with malignant nodules on the one hand or perhaps the hobnailed condition of atrophic cirrhosis on the other; but the bossy, lobular forms of the tumors, together with the previous history and other signs of syphilis, or, in the absence of both, the notable cachexia of cancer, if present, enable us to be pretty confident as to our differential diagnosis. In reasonable doubt an accurate blood count with differentiation of white cells will help us much. A decided and relative increase of lymphocytes and of eosinophile cells, according to Neusser or Cabot, would make this point very valuable. Of course, "a disappearance of the tumor after a tentative antisyphilitic treatment argues most positively in favor of gumma."[2]

So far as clinical symptoms go, syphilitic cirrhosis resembles one of the other forms. There may be jaundice and no ascites; there may be both ascites and jaundice.[3] On the other hand, there are instances in which neither sign is present. At an advanced stage, however, ascites can usually be determined; and what is of particular value is the localized pain in the right hypochondrium which is usually present. These pains are not constant, as a rule, but come on intermittently, or at all events are greatly intensified if previously they have been present in a mild, dull form. The pains during the exacerbations may become so intense as almost to resemble those of gallstones. If the disease has existed for a long while there is decided loss of weight, but scarcely ever to the degree which characterizes malignant disease. Constipation and various functional disturbances of the stomach and intestines are frequently present.

The congenital form of syphilis of the liver I do not remember to have met with; if I have my memory is too uncertain to be a faithful reporter.[4] By those who have seen or described it it is said to be a diffuse fibrosis, where the abnormal tissue formation penetrates into the

[1] Ibid. cit.

[2] Einhorn, Medical Record, August 17, 1901.

[3] Stockton states when jaundice occurs, even with apparent alcoholic cirrhosis, especially if accompanied by cachexia, it is well to suspect syphilis.—Medical News, June 28, 1902, p. 1244.

[4] According to Osler it "is rare and nearly always overlooked."

lobules or between the cells. The fibrous tissue is an immature development. The liver itself is large and it is accompanied by jaundice, ascites, and emaciation.[1] While as regards the pure pathology of cirrhosis, as Cheadle says, there is more or less unanimity among writers, this is not true of the causation of symptoms as connected with morbid anatomy, nor of the course and clinical manifestations of the disease in its various forms. One of the questions for settlement is to know whether the atrophic form is anything more than a later stage of the hypertrophic. Further, more definite judgment as to Hanot's biliary cirrhosis is desired, and as to whether hypertrophic cirrhosis is a real entity. These and many others are of singular interest. It is ordinarily accepted that atrophic cirrhosis is mainly caused by alcohol; indeed, that it is the essential cause in the vast number of cases. Still, malaria has seemed to be a sinning factor at times. Unfortunately, a typical case of malarial origin is rarely found, at least with us in New York. This may be accounted for, and doubtless is, by the relatively mild form of malaria from which we suffer. The æstivo-autumnal sort, with the characteristic crescents in the blood, does not occur often. They are relatively exceptional. Now, it is in just these cases or those of long-continued malarial cachexia, where we find great enlargement with fibroid induration of the spleen and also of other abdominal organs, notably the kidneys. Why, then, should we anticipate finding well-marked morbid effects of this sort in the liver if, as I do believe, the liver as an organ is not nearly so apt to be much affected by malarial poison as is the spleen? Also, I would state that it is most unusual for us to discover cases of profound malarial poisoning where we could absolutely eliminate the disastrous influence of alcohol from the equation; and yet it is stated, even by those who claim never to have seen a case of malarial cirrhosis, that there is nothing absolutely improbable in the assumption, inasmuch as malarial indurated spleen is fully determined. To my mind, this reasoning by analogy is very lame and inapplicable to the liver, in view of the fact of its very different structure and functions. When we consider how prone the liver is to become engorged and somewhat cirrhotic in all cardiac affections as well as in all obstructive lung diseases, it would seemingly be doubly reasonable to eliminate the malarial factor in causation, unless pretty

[1] Vide Cheadle. Lumleian Lectures for 1900. It affords me great pleasure in this connection to speak with admiration of these lectures, and to state that I have freely used them in writing this paper. Indeed, I have followed his outlines (Cheadle's) because I could find none better.

Since the above was written, Dr. George G. Sears and Dr. F. T. Lord have published in the Boston Medical and Surgical Journal of September 11, 1902, a very important paper on cirrhosis of the liver, based on all the fatal cases in the Boston City Hospital and the Massachusetts Hospital since 1896 in which the diagnosis was proved by histological examination. Many of their conclusions, according to the London Lancet of October 15, 1902, are only confirmatory of those published in England by Dr. Cheadle and by Dr. Hale White.

clearly evident. I direct particular attention to this statement, because I know that in most text-books malaria is insisted upon as a cause of atrophic cirrhosis of the liver. Osler,[1] in this connection, writes: "In our large experience with malaria during the past nine years not a single case of advanced cirrhosis due to this cause has been seen in the wards or autopsy-room of the Johns Hopkins Hospital." Now, it is well known that the malarial manifestations found in the city of Baltimore—a few indigenous, many coming from regions farther South—are more virulent than those we meet with in New York or other cities of the North in the United States.

Osler also writes,[2] in speaking of the liver: "Only those cases in which the history of chronic malaria is definite, and in which the melanosis of both liver and spleen coexist, should be regarded as of paludal origin."

There seems to be little doubt, also, that hypertrophic and atrophic *alcoholic cirrhosis* are distinct forms of disease and not different stages of the same form. This affirmation seems reasonable when we consider the very marked difference in the distribution of the fibrosis as well as of its nature in the two cases. In the one the affection is markedly multilobular; in the other it is monolobular in quite as pronounced degree. According to Cheadle, the error in confounding the two diseases arose originally from the hypothesis that Hanot's so-called biliary cirrhosis was simply the hypertrophic form. In many instances of cirrhosis of the latter form there is unquestionably a period when the liver is simply congested and enlarged, and yet no formation of abnormal fibrous tissue is yet begun, not to speak of any degree of contracture which later on may prevail. In these cases the liver is said to be much softer than it is where hypertrophic cirrhosis has become developed. This statement is no doubt true, and can be shown obviously in the autopsy-room on rare occasions. When it comes to actual clinical work and interpretation I am obliged to confess that this stated hardness as compared with softness, where the large liver is merely congested, is very difficult to differentiate. I have seen many cases of enlarged, smooth liver where there were few or no symptoms of ill health, unless, perhaps, slight evidences of dyspepsia should pass for such. In these cases the tactile sensations, so far as relative hardness is concerned, revealed little or nothing from this standpoint. This judgment is specially correct, I am confident, where the patient is corpulent, with thick abdominal walls, due to the deposit of adipose tissue. In spare, meagre individuals, with lack of muscular tone and relaxed abdominal walls, the problem to be settled is much easier, and we may indeed say, truthfully, "Liver is hard or liver is soft." Of course, we should never

[1] Practice, fourth edition, p. 570.

[2] Ibid. cit., p. 209.

expect to find in hypertrophic cirrhosis the extreme *hardness* to tactile sensations which is characteristic of the atrophic form; nor is it rational to expect it when we consider the very great difference which exists in the variety of the fibrosis—fine in one case, coarse in the other. The same cause—alcohol—which produces fibrosis of the liver also effects interstitial changes in other abdominal organs, and particularly the kidneys, which are thus affected in a large proportion of cases.

Despite the fact that it is affirmed that jaundice does not occur in atrophic cirrhosis, this statement cannot on inquiry and research be confirmed. On the contrary, it would seem as though we may and do have jaundice in all forms of cirrhosis. What is true is that jaundice occurs earlier in the hypertrophic form than it does in the atrophic, and hence, of course, when it does show itself in the latter form it is a sign of very bad augury. Many of the particular symptoms given by Hanot to designate specially his form of biliary cirrhosis are to be met with in the ordinary hypertrophic form, many of which are doubtless alcoholic; but when we come to consider the whole description of this writer we fail to find him in accord with other observers—mainly outside of France. Even the hyperplasia of bile ducts which Hanot considers so characteristic may be found in other forms. The jaundice does not always occur in the usual hypertrophic form, nor, again, is ascites always absent, and the spleen may not be visibly enlarged. Pain and pyrexia simply show advent of perihepatitis, and, although frequent in the hypertrophic form, it may also occur in other forms. Nervous phenomena and the typhoid state are more frequent in this form, but they are not absolutely distinctive. Chronicity is not constant, and, as we see, already, cases do not conform in all respects to a purely classical type. Where alcohol is a prominent factor in causation the symptoms approximate those of the atrophic form. No doubt in just such instances the hypertrophic liver is specially hard. The syphilitic liver, like the hypertrophic form, is often enlarged, extending in the right mammary line far beyond the right free margin of the ribs. If gummata are present they may be recognized, as already stated, by the distinct irregularities or bossing of the surface. If instead of gummata there is a cirrhotic process due to syphilis, the liver may also present a swollen appearance, and this is also true if amyloid degeneration has become manifest, which may be shown in advanced syphilitic conditions of the liver. In both syphilitic cirrhosis and amyloid liver the organ is hard and relatively smooth (Einhorn), and in the former case the fibrosis is said to be diffuse and monolobular. (Cheadle.) Not always is the syphilitic liver large; it may be small, and is thus often confounded with the alcoholic liver. This is especially to be regretted from a therapeutic standpoint, knowing as we do how invaluable antisyphilitic treatment is in these cases. Perihepatitis, while

not pathognomonic of syphilitic liver, occurs very frequently in connection with it. Moreover, in this form a similar condition is more apt to extend to other organs, particularly to the peritoneum, where it causes that adhesive inflammation which of itself is quite characteristic. Where syphilitic cirrhosis exists it may be more or less advanced. Indeed, its presence may only be revealed by a slight scarring of the free surface and some thickening of the hepatic capsule. Such pathological conditions may serve to fix a diagnosis post-mortem where there has been no syphilitic history and where signs and symptoms during life left one in reasonable doubt as to the etiology of the case. Inasmuch as syphilis of the liver is a late form of the disease, I have known instances where the patient seemed almost oblivious of his ever having had it, and where he could only with some difficulty be made to understand any connection between his previous history and his actual symptoms. I am now having in mind educated and fairly intelligent men of the world. This is a practical observation of importance from the point of view of insistence upon antisyphilitic treatment at times, even though the patient is skeptical and disposed to resist or follow out his own impressions of his ailment. No organ at times becomes more important in the history of hepatic cirrhosis than the heart. As soon as it shows symptoms even of dynamic inefficiency immediately there is a tendency to venous stagnation, which must promote growth of fibrous tissue and development of ascites. Alcohol, as we know, affects the heart as it does other organs; but here it seems rather, as a rule, to produce fatty or other degeneration of the muscular fibres than deposits in interstitial tissues. No doubt these cardiac changes account for many sudden deaths in syncope, or sudden asthenia otherwise unexplained. Frequent stimulation may tide over some of these attacks, but to be effective it must be employed without delay.

I have already indicated the effect of alcohol upon many abdominal organs. Of course, we can understand if these organs are much implicated their influence upon the rapid march of hepatic cirrhosis is greatly felt. Hepatic cirrhosis is particularly liable to be complicated with acute miliary tuberculosis of some organs, and very many patients die from this rather than the hepatic disease itself. In this way it is shown how imperative it is for these patients to keep up good nutrition and live all the while nearly in the open air. The statements of many observers corroborate this. Thus Osler writes: "In seven of my series the patients died with either acute tuberculous peritonitis or acute tuberculous pleurisy."[1] It is curious, on the other hand, that distinguished and careful clinicians like Flint and Fagge apparently make no note of it.

[1] Ibid. cit., p. 571.

The prognosis of hepatic cirrhosis has usually been most gloomy. Once ascites is revealed the patient's lease of life appears very limited. To-day we are more encouraged and regard certain cases very hopefully. Even in the advanced cases of atrophic cirrhosis we cannot always be sure to what extent some, not to say many, of the liver cells retain good functional power—at all events, power sufficient to help continue good nutrition if attending conditions be treated rationally.

It is recognized generally that we have no remedy which will make disappear the formation of fibrous tissue in the liver; but the ascites may be removed, even in these extreme cases, and allow the collateral circulation to act, with relief, to a certain degree, of the obstructed portal circulation. Then, every time effusion becomes considerable and organs are interfered with in their action through pressure, let paracentesis be repeated.

It has been shown by Fagge that cirrhosis often becomes quiescent before it reaches its final stage.[1] Flint seems to corroborate this view, because he says emphatically that life has lasted months and years after ascites had become developed and been recognized. Even in some atrophic cases of advanced type nutrition is still preserved, and this is always of good augury, because, despite the ascites, it shows some liver cells able to function normally. Of course, there is a possibility in these cases that we have not to do with a true cirrhosis of the liver itself, but with a perihepatitis or chronic peritonitis which was very probably the cause of the abdominal effusion. In this connection I would quote Fagge[2] again to corroborate my statement.

In hypertrophic and syphilitic cirrhosis the prognosis is much more hopeful. In the former case the development of fibrous tissue is of immature form, and occurs more rapidly with intercurrent conspicuous cell proliferation. This rapidly formed connective tissue is never so dense nor is it so destructive to the liver cells as that of the atrophic form of cirrhosis. In these cases there is often relative youth and good nutrition. Hence, from all these standpoints the prognosis is more favorable.

The prognosis of hepatic syphilis is even more hopeful. Of ten cases reported by Einhorn "only one patient died, and even this one had been considerably benefited for five or six months, whereas all the others were either perfectly cured or much improved."[3]

Of course, if cirrhosis could be recognized at an early stage, and before the advent of ascites, the outlook would not be immediately unfavorable. Sometimes we are able to make this diagnosis from

[1] Paper read before British Medical Association, 1883, vol. ii. p. 566.
[2] Practice of Medicine, vol. ii. p. 315.
[3] Ibid. cit.

certain prominent signs or symptoms: the indurated, large liver—an organ enlarged—and also irregular, vascular stigmata on the skin and face, and passing jaundice; an enlarged heart, constipation, dyspeptic symptoms, palpitations, and, it may be, some emaciation. We should act in accordance with the manifest indications, and among these is one primary and essential to correct absolutely—an alcoholic habit, if, as is usual, it has previously existed.

We often meet with combined cases of alcoholic and syphilitic cirrhosis. Some such cases have been known to recover during several years. This recovery was evident through subsidence of the ascites and recovery of the general health. (Cheadle.)

The first and most important indication of useful treatment arises from the point of view of arresting growth of fibrous tissue in the liver, and in this way the preservation of the remaining healthy liver cells. This is accomplished, if at all, by abandonment of the use of alcohol, which cannot be too urgently insisted upon in the great majority of instances. Of course, there may arise states of anæmia, prostration, or great weakness in which a moderate amount of good alcoholic stimulant may be imperatively required, at least for a time, and under such circumstances should surely not be withheld. This must be regarded merely as a temporary necessity, and we must have in view constantly the fact that it has been shown that even if fatty degeneration of liver cells be begun it will often be arrested if alcohol be wholly given up. A judiciously arranged dietary is only of secondary importance, and yet it is undoubtedly true that the digestive organs must be supplied with suitable food products, properly prepared, to sustain active nutrition and to ward off, as far as may be, certain functional or even organic disturbances in part dependent upon auto-intoxication of gastro-intestinal origin. Fats and sugars should be notably diminished in the dietary, for the reason that in the impaired liver functional power is decreased, and is shown especially in its inability for proper assimilation of foods containing many such elements. The simplest dietary of milk, eggs, stewed fruits, well-cooked fresh vegetables, and the lighter meats is of decided utility. Semmola's is the only rational treatment, viz., to reduce the quantity of food to a minimum and give it in a form which will tax the liver cells least. Milk is undeniably the best of all; but when this becomes intolerable, as it often does, eggs and other light food may be added. No doubt some instances of cirrhosis of the liver originate in auto-intoxication from the stomach and bowels. In all instances aggravation of the developed disease may result from it; hence over and beyond appropriate dietary the use of suitable antiseptic remedies like guaiaquin and benzosol (Gasper) may be formally indicated. Among drugs which have a decided action, and one most beneficial in almost all syphilitic cases, iodide of potas-

sium easily ranks first. There can be no question, in view of very many recorded cases, that gummata in their early stages are reabsorbed through its action. It is highly probable, also, that perihepatitis and similar conditions of other abdominal organs (spleen, peritoneum) are very favorably affected. It is not a sufficient reason to proscribe the use of the iodide because the syphilitic nature of the case is not always perfectly clear. In many instances doubt may legitimately exist. Indeed, in many combined alcoholic and syphilitic cases a positive differential diagnosis as to how much is due to alcohol, how much caused by syphilis, is impossible. The only safe rule, then, is to give up alcohol and take the iodide. Again, in instances where there is no history of syphilis and no evidence discoverable of its presence, it is yet wise at times to administer the iodide, the reason being that purely alcoholic[1] cases and those due to syphilis of the nature of an interstitial hepatitis are often confounded one with the other.

In the event of evidences of heart weakness, and in view of the well-known post-mortem findings, digitalis and heart tonics should be employed judiciously. Salines and diuretics are of some use in the relief of ascites, but, as a rule, are of more value in warding off its return for a while after paracentesis than in preventing the necessity of this operation. The explanation of this is not perfectly clear, although a theory for it may be readily offered, viz., that the absorbents relieved from pressure are more efficient.[2] Very active purgation by the use of hydragogue cathartics is at no time indicated, as it is useless and may become directly injurious by depleting the patient's strength very much or by bringing on diarrhœa often difficult to arrest. On the other hand, the moderate use of mineral waters to keep the bowels regular may be very necessary to the patient's welfare.

In the treatment of hypertrophic cirrhosis Nothnagel has wisely insisted upon small, repeated doses of calomel. Vaughan believes that later this form of disease will be treated mainly by surgery, as it is the only way by which the gall-bladder and biliary vessels can be disinfected.

Billings quotes Kussmaul as using chloride of ammonium to prevent proliferation of the connective tissue cells, and he (B.) claims in this way he has seen induration of the liver disappear as well as some local symptoms connected with the disease.

Whatever may have been the objections in former years to paracentesis, legitimate or unsupported, to-day it seems very clear that in early and repeated paracentesis the best hope of the patient lies. Even in

[1] Of the frequency of this form, one may judge from Flexner's report of autopsies done at the Philadelphia Hospital. Among eighty-eight cases of syphilis of the liver, forty had interstitial hepatitis.—Medical Record, October 19, 1901.

[2] Thromboses of the portal vein may cause rapid reaccumulation of ascites.

advanced instances of atrophic cirrhosis life is prolonged and suffering diminished; but in instances where we have an enlarged liver with ascites, which in such cases often occurs when the disease is not far advanced, we get our best results from paracentesis. The fluid may recur in smaller quantity after each paracentesis, and in some undoubted examples, after several operations, no fluid has recurred, and so far as symptoms are concerned, we may properly say a recovery has taken place. This may last for many years. I have had at least one such instance in my practice. The patient recovered from the ascites, and subsequently died of another disease than hepatic cirrhosis, as was evident at the autopsy. The danger to-day of peritonitis arising from paracentesis is very slight, indeed, if ordinary aseptic precautions be observed. I do believe it is wiser to employ the ordinary aspirator or Flint's modification of the Davidson syringe, than the trocar and canula, and mainly because the flow of fluid is easily regulated, and thus there is less danger of syncope or heart failure, which might be directly caused by too rapid evacuation of fluid where cardiac degeneration is present. This accident may also be obviated, as we know, by the prompt use of a binder as the fluid flows from the abdomen. The binder also is useful in delaying return of ascites. There is less risk of serious injury to the intestines with the small needle attached to the aspirator than with a moderate-sized trocar.

Unfortunately, paracentesis is not always thoroughly satisfactory. The canula may become blocked in different ways and for different reasons, not always easy to obviate. In our very desire to benefit our patient and withdraw most of the fluid from the cavity we may run the risk of wounding the intestine. Sometimes the cause of the obstruction of the canula is a piece of false membrane; again it seems to be the intestinal wall, and we must be careful not to injure it. In some instances where we expect to obtain a large quantity of fluid we really get very little, which is discouraging both to patient and physician. Occasionally it seems as though the posture of the patient was responsible for this, but I have found the difficulty to arise when the patient was sitting up and also when the patient was lying down.

Some authors have objected to paracentesis because, they say, after it the ascites recurs more rapidly, and that, besides the risks alluded to, it is very depressing through loss of albumin from the blood on every occasion it is performed. This objection has little or no value. as a rule, especially if the patient be in fairly good general condition, Of course, if the patient is very old and feeble, or the disease very advanced, paracentesis is likely to hasten the fatal termination. On the other hand, where the abdominal and thoracic organs have been

[1] British Medical Journal, 1883.

compressed or pushed away from their normal position by excess of abdominal fluid there is no question that the fluid should be speedily removed. Thus great distress is often relieved, the kidneys begin to function with renewed activity, and the general condition of the patient is notably improved. The lungs are enabled to breathe freely again, and the heart becomes regular and fails to intermit. While getting additional power very rapidly, cough, expectoration, hypostasis, and even pleuritic effusion due to upward pressure soon disappear. Sometimes after paracentesis there is more or less leakage from the abdomen through the hole made with the needle or trocar. This is often very annoying to the patient, as his clothes and bedding become thoroughly wet; and yet it may be useful in a few instances from the fact that the drainage continues for several hours after the operation is concluded, and from regions the needle could not reach. In this connection it is proper to refer to continuous abdominal drainage by means of a permanent canula left in the abdomen after the trocar is withdrawn. I performed this operation on one occasion, with apparently some good result; but the dangers from aspiration of air into the cavity, peritonitis, and suppuration are such that I felt later that better ultimate results could be expected from repeated puncture and before the fluid was permitted to reaccumulate in too large quantity, or caused any notable distress, or interfered much with the healthy function of any important organ.

"The removal of fluid by continuous drainage has been practised with some success by Dr. Caille and Dr. Elliot in America, and by Dr. Urso in Italy."[1] And certainly in some cases it would appear to be safer and quite as effective as the radical operation to produce new anastomoses.

On the other hand, Weir,[2] who used permanent drainage in connection with or rather subsequent to the radical operation, "would hereafter prefer to resort to paracentesis if it became necessary, as the risk seems less."

It is surprising at times to remark the powerful diuretic effect of paracentesis. Kidneys that previous to it were inactive become active, urine that was albuminous, of high specific gravity, and contained casts accompanied by uræmic symptoms, has changed remarkably. The flow of urine has wonderfully increased in quantity, and its characters have become almost normal, while all uræmic evidences have soon disappeared. Without the paracentesis both purgatives and diuretics seemed wholly worthless to produce these much-desired effects.

If we wish to get the best effects from repeated tapping we must have patients under our immediate care, so that they may be tapped again

[1] Cheadle, p. 88. [2] The American Journal of the Medical Sciences, 1899, p. 723.

when the proper moment arrives. Tapping should be repeated in proper cases until fluid ceases to reaccumulate. During this period it should be our effort to maintain the patient's nutrition to the highest degree possible. Through constant care and attention we obtain the best results; through carelessness or permitting the patient to absent himself too long from observation we have often cause for regret, and the patient relapses into an impoverished and threatening state.

On the other hand, Hale White's observations would go to show "that in the cases of cirrhosis of the liver with chronic peritonitis the survival for a considerable length of time was due to the fact that the latter lesion assists in some way in the formation of a collateral circulation."[1]

Now, as Osler writes: "We know that extreme grades of contraction of the liver may persist for years without symptoms when the compensatory circulation exists. The so-called cure of cirrhosis means the re-establishment of this compensation."[2]

Upon this idea of re-establishment of this compensation rests the modern radical surgical treatment of cirrhosis of the liver. The method is to promote adhesions between the liver, spleen, and abdominal walls and diaphragm, thus helping collateral circulation by new vascular channels. This is attempted, first, by completely evacuating the abdominal contents, and then, by thorough scrubbing of the organs referred to, set up a certain amount of irritation which shall tend to make the formation of new vessels more probable. In this connection Cheadle is of the opinion that if we consider the conditions where the new vessels are found naturally they do not seem favorable, being associated with the worst cases, and do not lead one to try to produce them artificially. Opposed to this view we would cite three cases cured: one of Osler's,[3] operated on by Dr. Bloodgood at Johns Hopkins Hospital; another of Brown's,[4] another of Frazier's.[5] In one instance under my care, operated on by Dr. F. H. Markoe, nearly two years ago, the patient has had recurrent ascites, necessitating repeated tappings since the radical operation. Two of Osler's cases were unsuccessful. As regards one or two tappings after the operation, this we should expect where a drainage-tube has not been introduced, the reason being that time is required for the formation of adhesions and new veins; and the introduction of the drainage-tube is now shown to be bad from a surgical standpoint, as it opens a channel of infection. (Frazier.)

In Dr. Brown's successful case, at first referred to in the *Presbyterian*

[1] THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, March, 1901, p. 259.
[2] Ibid. cit., p. 566.
[3] Ibid. cit., p. 577.
[4] New York Medical Record, October 19, 1901, p. 637.
[5] THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, December, 1900. p. 661.

Hospital Reports for 1900, and the patient subsequently presented at a meeting of the New York State Medical Society, held October 16, 1901, at the New York Academy of Medicine, the condition was one of atrophic cirrhosis, due to alcohol. There was no syphilis and no malaria, although the spleen was enlarged. There was no pronounced venous engorgement on the abdominal walls. The patient was operated upon over two years ago. There has been no recurrence of ascites, and the nutrition remains good. The patient is doing his usual work—that of a day laborer.

Frazier[1] in the remarks he makes, prompted no doubt by a successful case, wisely insists, as a *formal* contraindication to the operation, upon the absolute lack of functional power in the liver cells—*i. e.*, shown usually by extreme atrophy. (Packard.) In his judgment, the presence of cardiac and renal degeneration is only a relative contraindication. He also states that it is essential, in order to avoid fatal toxæmia, that the collateral circulation should be formed gradually. Where the cases have been carefully selected he "believes the operation has a future."

Fourteen cases are thus far reported, seven of which appear to have been materially benefited or cured by the operation (Brown) and three died from the operation.[2] "The many instances of practical cure following tapping, and the uncertainty of the exact pathological state of the liver, together with the somewhat formidable character of the operation and liability of infection, invest the operation at present with a large element of doubtful expediency."[3] These remarks, cited textually from Dr. J. D. Bryant's work on *Operative Surgery*, appear to me eminently wise.

In all these cases, moreover, it is judicious to properly estimate the amount of functional disturbance, if possible, of the liver cells (icterus, acholic stools, urobilinuria, etc.) as well as the physical changes of the liver itself. In it may be found, as Brown says, a formal contraindication to the wisdom of the operation. Neumann[4] also wisely insists "that the liver cells be not too greatly impaired in their functional capacities, and that every precaution should be taken in selecting proper cases, in order not to permit discredit to fall upon so valuable an operation."

Brown "feels assured that the great risks attending operations on advanced and failing cases will be notably wanting in similar procedures applied in earlier stages of the disease."[5] No doubt this state-

[1] Loc. cit.

[2] Later Packard reports twenty-two cases, with nine recoveries and eight deaths (THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, March, 1901, p. 265), and in a "note" one death—one doubtful.

[3] Bryant, Operative Surgery, 1901, vol. ii. pp. 802, 803.

[4] Quoted by Brown (p. 11).

[5] Page 16.

ment is correct, but in my judgment it is correct only so far as it applies to all important or dangerous surgical procedures. The great difficulty is to convince the pure physician with the facts as reported up to date, and allowing for errors of diagnosis with respect of the precise nature of the liver condition and for the concomitant conditions almost always present (heart, kidneys, spleen, pancreas, etc.) that such a stand is justified. I am scarcely of that opinion until it be shown that the radical operation in similar instances gives better results than the far less serious procedure of simple and repeated paracentesis.

Dr. Weir's standpoint appears to be a more rational one, viz., "The operation was worthy of trial in apparently hopeless cases of liver cirrhosis in which the abdomen rapidly refilled after repeated tapping, and in which the large quantity of the fluid was producing fatal exhaustion."[1]

Dr. McBurney in discussing Dr. Weir's paper thought that analogy with what occurred after simple incision in cases of tuberculous peritonitis allowed one to question whether the relief of ascites in cirrhosis of the liver which followed the radical operation was brought about by the development and growth of vascular anastomoses. This view of McBurney's seems to approximate that of Dr. Osborne, of New Haven, and of Dr. Cheadle, already cited.

On the other hand, Packard and Le Conte[2] claim that "one of the ways by which repeated tappings may aid in the recovery of cases of cirrhosis of the liver is through the formation of adhesions similar to those aimed at in the operative procedure, but to a less degree." Be these views as they may, I cordially assent to their previous statement,[3] that "these cases of advanced cirrhosis of the liver, operated on or not, die with evidence of progressive toxæmia and gradual failure of all the organs to do their proper work."

Despite these views, they state in their conclusions, as their opinion, "that where the diagnosis of pure portal cirrhosis of the liver can be made, and where persistent and well-directed medical treatment is productive of insignificant results, the operation should be strongly recommended."

Here, it seems to me, the great difficulty lies in this precise diagnosis at the present time; for do we not know that constantly our autopsies show that concomitant lesions exist which render nugatory all radical operations—*i. e.*, other kinds of cirrhosis, chronic peritonitis, advanced degeneration of other organs, like the heart and kidneys, etc.?

There can be little doubt that in very many cases of hepatic cirrhosis it is important to do what we can medicinally and otherwise to

[1] New York Medical Record, January 28, 1899, p. 143.

[2] The American Journal of the Medical Sciences, March, 1901. [3] Ibid., p. 257.

keep the heart in a vigorous state. Once it becomes inefficient functionally, either because of simple dynamic weakness or owing to structural changes, the development of the ascites is certainly more rapid and more apt to recur. We recognize in this way that the obstructed portal circulation due to fibrosis is also heightened notably by venous stagnation caused directly by impaired heart power. No doubt the explanation of instances of early effusion in hypertrophic cirrhosis is thus often satisfactorily given. If such a view be admitted it can be readily understood why we can obtain good effects from suitable treatment in just such cases. An important part of this treatment must be the maintenance of sufficient cardiac power if it be possible to prevent venous stagnation in the liver.

In instances where venous stagnation occurs of cardiac origin the hepatic veins at the centre of the lobules are especially affected, and it is also true in these instances that here is likely to be formed the fine fibrous deposit which, as we have seen, characterizes hypertrophic cirrhosis. Not always is the cardiac inefficiency shown by evident physical signs, nor, indeed, by the presence of ascites; still, in hypertrophic cirrhosis or simple engorged liver it is a safe plan to give, for a while at least, small, repeated doses of digitalis, and note its obvious effects either on the size of the liver directly or some of the suggestive symptoms connected therewith.

Appended are histories of cases of "omental anastomosis."

Case I.—Case of cirrhosis of the liver in which radical operation was performed by Dr. F. H. Markoe. J. S., aged fifty years, married; hotel steward; born in the United States; admitted to St. Luke's Hospital June 30, 1898. Alcoholic history; suffering from ascites. Liver probably enlarged; rough and nodular. Abdomen much distended; evidences of fluid; superficial veins enlarged.

First Aspiration. Three days after admission, 125 ounces obtained; second: eleven days later 128 ounces obtained.

Treatment nil. Left hospital July 22, 1898; re-entered, December 6, 1898.

Abdominal fluid increased in quantity as compared with quantity before the last tapping, July, 1898.

Third Aspiration. Two days after admission, 370 ounces obtained; fourth: five weeks after admission, 400 ounces obtained; fifth: seven and a half weeks after admission 440 ounces obtained; sixth: ten and a half weeks after admission, 475 ounces obtained.

Treatment. Digitalis, iodide of potash, theobromine, copaiba, etc. Left hospital March 1, 1899, and readmitted two weeks later; abdomen greatly distended.

Seventh Aspiration. Day after admission; 390 ounces obtained. Left hospital, and readmitted April 17, 1899.

Eighth Aspiration. Day admitted; 426 ounces obtained.

May 13th. Ninth: 390 ounces obtained.

June 14th. Tenth: 450 ounces obtained.

July 10th. Eleventh: 330 ounces obtained.

August 12*th*. Twelfth: 452 ounces obtained.
October 7*th*. Thirteenth: 520 ounces obtained.
November 14*th*. Fourteenth: 510 ounces obtained.
Treatment. Codeine for cough.

January 22, 1900, Dr. F. H. Markoe performed upon the patient the operation of "omental anastomosis," and 500 ounces of light yellowish fluid slowly evacuated from the abdomen. On palpation, the liver was found large; also some abdominal adhesions. Vomiting of green fluid off and on for six days following operation.

Fourteenth Aspiration. Six weeks after operation; 138 ounces obtained.

Subsequently, up to November, 1901 (twenty-two months later), patient has been aspirated about fifteen to seventeen times, which, with those performed before operation, make about thirty in all.

November, 1901. He is now confined to bed, and is unable to leave it by reason of asthenia.[1]

Case II.—A second case of "omental anastomosis" for cirrhosis of the liver was performed by Dr. F. H. Markoe at St. Luke's Hospital, April 27, 1901. The patient had marked ascites; was a boy, aged thirteen years, and had been quite a drinker. Subsequent to the operation the patient was tapped once before he left the hospital, on May 21, 1901. Since that date he has returned about every six weeks to have the fluid removed from the abdominal cavity. The patient's general condition is about the same as before the operation. The ascites is probably somewhat less.

Case III.—The following case of "omental anastomosis" is one in which Dr. F. W. Murray operated.

History. P. A. B., married, aged forty-eight years; no specific disease; excessive alcoholic habits.

Four months before admission to St. Luke's Hospital patient noticed yellow conjunctivæ and loss of flesh and strength. His abdomen increased by eight inches in size. This increase subsided for a time under calomel and salines, but soon returned. April 2, 1900, entered hospital; 328 ounces of fluid removed by tapping; largely reaccumulated in two or three days. Transferred to surgical service April 18th.

Abdomen measured 44½ inches at a point three and a half inches above the umbilicus; percussion flat over the whole abdomen. Operation April 19th, by Dr. Murray. Incision four inches long at the left of the umbilicus; 3¼ gallons of fluid removed; omentum thickened and vessels injected; sutured to parietal peritoneum by five interrupted sutures of No. 1 catgut; stood operation well. Urine acid; specific gravity, 1020; slight trace of albumin; no sugar; few hyaline casts.

Aspirated April 23, and 64 ounces of fluid obtained. April 30th, circumference 39 inches. May 2d, primary union of wounds. May 12th, œdema of feet; stuporous; pulse rapid; coryza marked; erythema over nose, diagnosed as erysipelas. May 13th, temperature between 98.3° and 99° F. Pulse varies from 90 to 100. Respiration, 24. Died. (Above history furnished by Dr. Martin.)

Note.—Since writing the foregoing paper a valuable contribution from the pen of Dr. George E. Brewer, on "The Surgical Treatment

[1] Patient died December 15, 1901, from heart failure.

of Ascites Due to Cirrhosis of the Liver," has been published. From it we take the report of "5 personal cases and analyses in tabular form from about 50 more from the literature." From reviewing these statistics Brewer finds at least 6 patients who have been cured of ascites by this procedure—*i. e.*, Talma-Morrison operation—and who have remained well for two years or more; 6 others have died, with relief of this symptom from two to six months before death, or who had not been under observation long enough to demonstrate a permanent cure. Another patient suffering from hemorrhage of the alimentary canal was promptly cured by this operation. Many others have been materially benefited; 38 have recovered from the operation; and, considering that the great majority of these were within a few weeks of inevitable death, he thinks that it should encourage us to suggest operation at an earlier and more favorable stage of the disease. If this suggestion is followed he believes that statistics will show a great improvement over those he is able at this time to present."[1]

In a later contribution on this subject Dr. W. Murrell, of Westminster, writes[2] that "much depends on careful selection, and the best results would probably be obtained in the pre-ascitic stage when the diagnosis rests on the alcoholic history, with hæmatemesis and enlargement of the liver and spleen."

A CASE OF MULTIPLE MELANOTIC SARCOMA UNSUCCESSFULLY TREATED BY X-RAYS.

By James P. Marsh, M.D.,
SURGEON TO THE SAMARITAN HOSPITAL, TROY, N. Y.

The X-ray treatment of various malignant diseases has been used long enough to thoroughly establish the great utility of the method in certain cases and locations. For the ordinary slow-growing epitheliomata of the skin the X-rays are practically specific if the treatment is instituted before glandular involvement has occurred. In my own cases I have not failed to apparently entirely eliminate this disease in from eight to twelve sittings of ten minutes each—I say apparently, because the time elapsed has not been sufficiently long to call the condition a cure; and the X-ray therapeutist should be willing to apply the same three-year rule to his work as does the general surgeon.

But however firm, therefore, our conviction that the X-ray is of inestimable value in the above-mentioned conditions, there is an equally strong feeling that certain malignant tumors have been made

[1] Journal of the American Medical Association, February 22, 1902, p. 135.
[2] Lancet, June 7, 1902, p. 1604.

worse thereby. Several times during the course of X-ray treatment of cases of recurrent cancer of the breast I have felt that, although the local condition has been much benefited, metastases in the internal organs occurred much more quickly than they used to do under the old methods of treatment. So strong had this feeling become that I had decided to have the question of leucocytosis investigated during the time of X-ray treatment as soon as a suitable case should present. As such a case has just passed through my hands, and as the blood examinations show a steady fall in the number of leucocytes with each treatment, I have thought the case worthy of being placed upon record at once. As it is a case of a fortunately rare disease, and intrinsically interesting, it is reported somewhat *in extenso*.

C. H. M., referred to me by my friend Dr. W. J. Hunt, of Glens Falls, N. Y., entered my service at the Samaritan Hospital, July 2, 1902. He is of the white race, aged fifty-two years, and by occupation a teamster. He was born in the United States, and is married.

He complains of numerous tumors upon various parts of his body, but mainly upon the left side of the back, overlying the left scapula and extending thence into the axilla and around upon the forepart of the chest; of pain in the left shoulder, and of limitation of motion in the left shoulder and left arm.

The patient's father died at the age of sixty-three years, of consumption, and his mother died at the age of sixty-four years, of apoplexy. His only brother died at the age of twenty-two years, of rheumatism, and he has one sister who is living and well. No family history of tumor or cancer can be obtained.

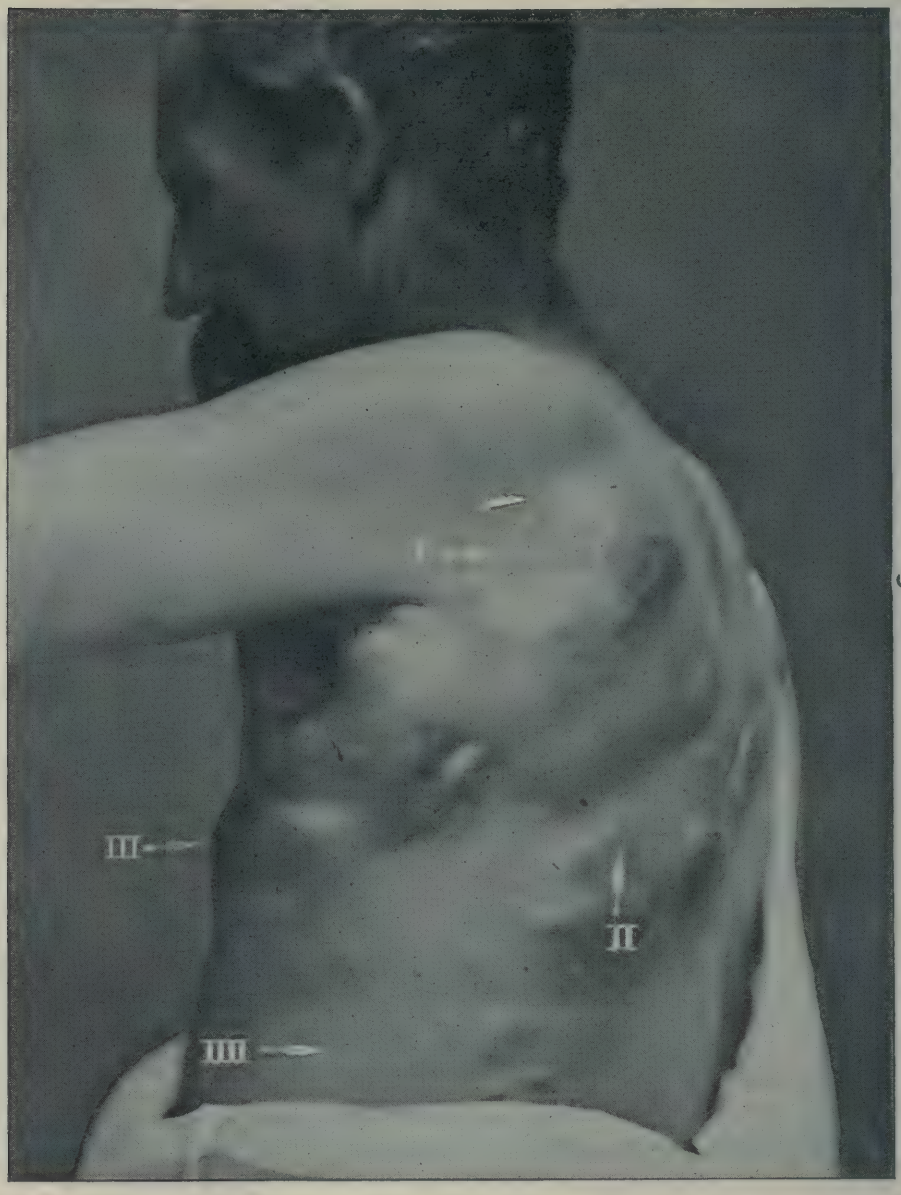
He has had all of the usual diseases of childhood. In adult life he had diphtheria, but otherwise has been well. He has used tobacco moderately, but has not used alcohol. At twenty years of age he had specific urethritis, and also again when he was twenty-three. He has never had syphilis. Upon several different occasions he has been confined in the Utica State Hospital for the Insane, for a report of which see below.

His mental apprehension is very faulty; but, according to his own statements his present trouble began about eight years ago, when a small black mole appeared upon his back, in the region of the angle of the scapula. This mole gradually enlarged, and finally, about two years ago, it became so large that the clothing would rub the skin from it, and it would bleed. This was very annoying, and as it had reached a diameter of one-half inch, the patient had it removed on January 1, 1902. He says that the mole was cut off level with the skin, and he is sure that at that time there were no tumors anywhere on his body. This operation, patient says, was done under cocaine, and that immediately thereafter the tumors appeared in the axilla and upon the front part of his chest. About one week after the first operation the mole was again excised, skin being taken with it at this time. On January 24th he was again operated upon, this time under ether, and the base of the mole and two tumors were taken out. After this operation the original site of the mole did not heal, and the region was again excised, after which it healed.

The patient's present condition is best shown by the accompanying photograph, the measurements being found below.

I. Large mass over scapula, marked I, measured, as the arc of a segment, 16 cm.

II. Subsidiary mass of four nodules, marked II, measured, as an arc of a segment, vertically, 20 cm.; transversely, 10 cm.



III. Axillary mass, marked III, measured, as the arc of a segment, vertically, 16 cm.; transversely, 21 cm.

These masses are firm in consistence and do not fluctuate. Where the skin is stretched tightly over the tops of them they are seen to be of a dark blue hue. At many places over the patient's body are numerous small, freely movable masses, which feel like bullets beneath the skin, and which vary in size from 1 mm. to 1 cm. in diameter, and

they are seen through the skin to be blue in color. A collection of these small tumors is seen in the photograph and marked III.

Physical Examination. The man is of medium height and of fair muscular development, slightly anæmic and slightly emaciated. His expression is anxious.

Lungs. The chest expands symmetrically excepting as regards the growths mentioned above. Palpation and percussion are negative. Auscultation reveals submucous râles throughout the left lung and in the lower lobe of the right lung.

Heart and Arteries. The arteries are slightly atheromatous. The superficial area of cardiac dulness is 7 cm. vertically by 4 cm. transversely. Obliterated apex-beat is found in the fifth space, inside the nipple line. All valvular elements present and in normal position. There are no murmurs.

Liver. Dulness begins at the sixth rib and extends downward 10 cm. to the free costal margin.

Abdomen. Nothing abnormal can be discovered in any part of the abdomen excepting in the left hypochondriac and the left anterior and lateral lumbar regions. The free margin of the right lobe of the liver cannot be palpated. In the left hypochondriac and the left anterior and lateral lumbar regions is a mass, estimated to be about 10 cm. in diameter, which does not blend with the liver dulness. There is no splenic dulness in the normal position. The most prominent part of this tumor is situated midway between the left anterior axillary line and the left nipple line, and is on a level with the umbilicus. There is no area of tympanitic resonance between said tumor and the muscles of the back. Over the most prominent part of the tumor it is dull, and this dulness shades off into the general tympanitic resonance of the abdominal cavity. When one hand is placed in front and the other in the loin the tumor lifts easily, but its range of motion is not great. Its margins are thick and rounded, and no notch can be felt therein.

Nervous System. Patient's mental comprehension is very much delayed. The cranial nerves are intact. The superficial and deep reflexes are present. Sensation is normal. All of the muscular movements are normal.

Diagnosis. Multiple melanotic sarcoma.

Through the courtesy of my friend Dr. E. G. Stout, of the staff of the Utica State Hospital, I am able to furnish an abstract of the history of this patient while in that institution.

Case No. 21,801. Admitted into this institution for the seventh time on July 24, 1901, the diagnosis of the mental trouble being recurrent mania. After his last discharge the patient had been well behaved and steadily employed until July 17, 1901. Upon that day, after having spent several days at work in the hot sun, he became noisy, talkative, restless at night, and very much excited. He would change his position with great rapidity, glance about him in a suspicious manner, and talk to himself at times in a loud tone of voice. These were the only symptoms which he manifested. Upon admission to the hospital he was quite excited, talked to himself, glanced about the room as though he were in fear of some person, and was unable to make an intelligent reply to a direct question. For some days he continued in

an excited and restless state, and was unable to concentrate his attention upon any work or pastime. At table he would play with his food or throw it about the room. In the course of a month or two there was a gradual improvement in his condition, and he was, in October, transferred to one of the farm colonies about a mile from the central hospital.

On January 10, 1902, the patient was anæsthetized and twelve enlarged glands were removed from the left half of the thoracic wall and the left axilla. Two of these glands were adherent to the skin, and in the neighborhood of one lying near the ninth dorsal vertebra, and to its left, was a growth almost one inch in diameter and of a friable character, which bled profusely. A large gland situated near the posterior border of the axilla at its base was closely adherent to the skin and somewhat inflamed. The same was true of three glands situated just external to the growth mentioned above. The axilla was thoroughly cleansed of tumefied tissue, and so much traumatism had occurred in the process that it was deemed best not to close the wound. It was not possible to approximate the edges of the wound when the skin had been removed. The wounds gave no special trouble and were healed at the end of three or four weeks.

On February 21 a case note states that the growth near the inner border of the scapula has again made itself troublesome by reason of its increased size. It was to-day removed, the patient having had the region anæsthetized by means of cocaine injections. At the same time a subsidiary growth a short distance below was taken out. The main growth was about the size of an English walnut, and the lesser one about the size of a bean. Again on March 20th, a case note states that secondary growths are making their appearance at all the points at which they formerly existed, excepting that in the middle of the back. The axillary glands are very hard, and are adherent to the skin.

April 19th. Tumors have increased in size very markedly, and patient is now inconvenienced by wearing his sleeve on his left arm.

On April 24, 1902, he was discharged from the hospital, having regained his usual mental condition.

Examinations of his urine upon several different occasions showed it to be normal.

During his stay in the hospital there was an evening temperature of from 99° to 99.8° F. His pulse rate varied from 82 to 108, and his respiration from 20 to 30.

He entered the Samaritan Hospital June 30, 1902, and he received his first X-ray treatment the same evening. As the technique employed was the same during each treatment I will give it but once.

The patient was placed upon his right side, the left arm being carried out from the body as near to a right angle as possible, in this way bringing the hemisphere of rays upon as many of the growths as was possible. A lead mask was placed over the face. The source of energy was an ordinary 110 volt, direct current. The coil was a twelve-inch Queen to which about three ampères of current were supplied. The tube was a Sayen tube, the surface of which was placed about two and one-half inches from the surface of the nearest growth. The vacuum of the tube as measured in air was six inches, time, ten minutes, with target over the tumor marked I in the photograph.

Herewith are presented the dates of the exposure and the blood examination following:

June 30th. First X-ray.
July 2d. Hæmoglobin, 60 per cent.; leucocytes, 22,500.
3d. Second X-ray.
3d. Hæmoglobin, 62 per cent.; leucocytes, 17,812.
5th. Third X-ray.
6th. Hæmoglobin, 63 per cent.; leucocytes, 16,000.
7th. Fourth X-ray.
8th. Hæmoglobin, 65 per cent.; leucocytes, 14,500.
9th. Fifth X-ray.
10th. Hæmoglobin, 63 per cent.; leucocytes, 12,000.
A note of this date says: "A great many more tumors have appeared, and those that were present have increased very much in size and in darkness of color. The patient has become very much weaker, and has to have hypodermics of morphine to relieve the pain arising from the above-referred-to growth in the abdominal cavity."

It seemed as if the X-ray treatment was having a direct detrimental effect, and in the interest of the patient it was discontinued. The patient was accordingly discharged from the hospital unimproved July 14, 1902.

When in Philadelphia, in March, 1902, my friend Mr. Wilbert, of the German Hospital, expressed himself to me as having a very strong conviction that large, rapid-growing sarcomata were accelerated in their growth by the application of the X-rays, and it occurred to me at that time that possibly it would be found that in these cases the leucocytes, the natural defenders of the organism, were rapidly diminished by the employment of the rays. This apparently is what did occur in the case above detailed. To be sure one case does not constitute a rule, but I would earnestly urge X-ray therapeutists to have their work in this class of cases checked up by a frequent examination of the blood, especially as regards the leucocytosis. It also seems to me that our physiological friends should furnish us with a careful study of the effect of the X-rays upon the blood condition of the normal individual.

MIXED TUMORS OF THE THYROID GLAND.

By Leo Loeb, M.D.,
of Buffalo, N. Y.

(From the New York State Pathological Laboratory, Buffalo, N. Y.)

Mixed tumors have been found in the following places: in the ovary and testicle, in the kidney, and in the salivary and lacrymal glands. They have also occasionally been found in the cervix uteri and in the vagina, in the bladder, and in other places. It will, therefore, be seen that mixed tumors occur mainly in glandular organs. It is further noteworthy that the mixed tumors in the various glands have, within certain limits, each their characteristic constituent tissues.

The mixed tumors of the generative glands are the most complicated ones, containing frequently parts of different organs and tissues. The kidney tumors contain glandular structures situated in sarcomatous tissue, and frequently striated muscle fibres. A combination of cartilage and epithelial or endotheliomatous formations is characteristic of the tumors of the salivary glands. The mixed tumors have always had an especial significance in so far as their existence served as an argument in favor of the origin of tumors generally from displaced embryonal cells. Wilms especially has lately reviewed the mixed tumors of different organs, and has tried to show that they are all essentially of the same nature. He explains all mixed tumors as originating from embryonic cells, either actually displaced or at least functionally detached from their normal environment. These cells may later on give rise to mixed tumors. The different tissues found in one mixed tumor are, according to him, all derived from cells ceasing to develop at one stage of embryonic life. The earlier this stage is the greater is the variety of tissues these cells are able to produce; and each cell has the power to produce a tumor-like formation containing all those cells which also in the course of normal development would have been produced by it. This conclusion does not seem to be absolutely justified by the facts gained by experimental embryology. It presupposes that each embryonic cell has only (to use a term of Driesch) that *prospective potenz* which under the conditions of normal development it really displays; therefore Wilms assumes that a mixed tumor of the kidney —*e. g.*, which consists of gland structures (of mesodermal origin) and of striated muscle fibres—must be derived from cells of an embryonic stage, where the differentiation into the Wolffian body and in the myotome had not yet taken place, therefore, from what he terms a "mesoderm cell." This assumption presupposes that a cell even under changed conditions of development can only give rise to the generations of cells it would have formed under normal conditions. This, however, does not seem to be the case. It is well known that isolated blastomeres up to the sixteen-cell stage proceed in their further development not as parts of a whole organism forming the specific tissues or organs they would have produced if they had remained in connection with the other blastomeres, but they continue to develop as whole embryos. An ovum developing under the influence of one-sided pressure gives rise to normal embryos; also no specialization of the first blastomeres under these conditions seems to have taken place. Experiments with the injection of teased embryonal tissues into adult animals (Féré, Birch-Hirschfeld and Garten, Galleotti and Ville Santa) are not conclusive in their results with regard to this question. It is uncertain which of the tissues which can be found later on have really developed from cells which would have formed these tissues also under

normal conditions. Of great importance, however, seem to be the recent experiments of Spemann. He found in triton, at a stage when the medullary plate is already indicated, that by tightening a ligature across the medullary plate the anterior end of the posterior part will form a head just as the anterior part will do. Under these conditions ear vesicles can be formed from parts which, if the development had proceeded normally, would not have formed any part of the head. Through injection of isolated cells such structures have not yet been formed. Probably the connection of these cells with a large part of the embryo is necessary for this result. At a somewhat later stage of the embryonic development a new head is not formed at these places. So much can be concluded from these experiments that the "prospective potenz" of embryonic cells under certain conditions is larger than could be recognized without experimental tests. *It is therefore at present not possible to determine from the composition of a mixed tumor from what kind of embryonic cells such a tumor is derived. It also proves that heterotopic formations are not of necessity produced by displaced blastomeres.*

Mixed tumors may from the beginning be malignant, or may after an apparently benign period assume this character. The facts known at present do not offer any explanation for malignant growth. Experimentally, displaced embryonic or adult cells have not been found to produce malignant tumors. Some thus far unknown factor must therefore be added to produce malignant tumors out of such cells if the displacement (or functional disconnection) plays any essential part at all in the production of mixed tumors. Wilms himself admits that some other factor besides the disconnection of cells may have to be present for the production of a tumor, although, at other places, the mere fact that these disconnected growing cells do not find the tension of their normal environment opposed to them seems to be sufficient to him to explain the malignant growth. Further, Wilms believes that all mixed tumors are of embryonic origin, owing to displacement or functional disconnection of embryonic cells, even if these tumors do not manifest themselves until later in life. Because there exist transitional tumors connecting complicated mixed tumors with simple sarcomata, these simple tumors have, according to Wilms, to be explained on the same basis. Wilms does not apply this conception to carcinoma, for which he admits a different etiology. This theory of Wilms as to the origin of *all* mixed tumors from displaced or functionally disconnected cells is, of course, not proven, although it is probable in the case of a number of tumors. There are, however, certain mixed tumors for which this explanation is improbable, namely, the mixed tumors of the thyroid gland.

The mixed tumors of the thyroid gland which I have found recorded

are of two kinds. There are, first, three undoubted cases of mixed carcinoma and sarcoma, and two doubtful cases. I shall report here a further case of carcinosarcoma in which there can be no doubt about the diagnosis. Secondly, I have found records of two tumors composed of sarcomatous tissue and bone.

The cases of carcinosarcoma reported are the following:

CASE I.—C. Kaufmann, in "Die Struma Maligna," describes a tumor in a man, aged sixty-seven years. The left lobe of the thyroid presented the appearance of a follicular struma. The right lobe, considerably enlarged, reached from the hyoid to the jugulum, and consisted in the centre of fibrous tissue. Around this fibrous nucleus, and especially toward the trachea, the tumor was a spindle-shaped sarcoma. The periphery toward the right side presented the appearance of a typical carcinoma, occasionally including normal gland structure. The zone where sarcomatous and carcinomatous tissue met was small; the sarcoma cells replaced here the ordinary connective tissue stroma which surrounded the carcinomatous alveoli. The interstices, which were filled with sarcomatous tissue, were enlarged. The carcinomatous alveoli were well defined toward the sarcomatous tissue. There were (metastatic?) nodules present in the periphery of the kidneys.

CASE II.—E. Kummer, "Sarco-adénome du Corps Thyroide ayant Simulé une Strumite Simple." The patient, Mrs. P., aged fifty-five years, had suffered for several years previously from a thyroid which slowly increased in size. A month before operation the growth began to increase rapidly. The left lobe of the thyroid only was affected, the right lobe being normal. The tumor consisted in the periphery of vesicles lined with cylindrical cells and including colloid. In the central part there could be found between the glandular parts large fusiform or oval cells separated from each other by very little intercellular substance. This interglandular tissue became larger further away from the periphery. At other places sarcomatous cells only were found, and again at other places only tubules consisting of cylindrical epithelial cells. These tubules were pressed against each other, no connective tissue being present between them, and the membrana limitans being preserved. A vein in the anterior part of the tumor was occluded by a thrombus consisting of fibrin and adenomatous tissue with cylindrical or cuboidal cells. Clinical symptoms suggested the presence of metastases in the lungs. No autopsy, however, could be obtained. From an anatomical point of view, Kummer designated the epithelial part of the tumor as an adenoma and not as a carcinoma, and believes it to be derived from the parathyroid rather than from the thyroid. Clinically, however, it was malignant. Of special interest is the fact that only one lobe, namely, the left, was affected.

CASE III.—H. G. Wells, "Multiple Primary Malignant Tumors: Report of a Primary Sarcocarcinoma in the Thyroid of a Dog, with Mixed Sarcomatous and Carcinomatous Metastases." This tumor was found in a Skye terrier bitch, twelve years old. The tumor affected both sides of the thyroid gland. The epithelial part of the tumor consisted of alveoli which were partly filled with colloid material, partly with cells. These alveoli were separated from each other by the ordinary connec-

tive stroma. The sarcoma consisted of spindle cells, mostly arranged perpendicularly to bloodvessels. There were many vessels and many karyokinetic figures present. As a rule, connective tissue separated the carcinomatous and the sarcomatous parts, but in some places the sarcoma infiltrates the carcinoma. In the cervical glands the metastases were carcinomatous. In the lungs, which were filled with metastatic nodules, most of them were pure carcinoma, some mixed carcinosarcoma. Kidney, heart, and small intestines showed sarcomatous nodules.

CASE IV.—A further case I observed in a white rat. I used the sarcomatous part of this tumor for transplantations, and have therefore referred to this tumor in the paper describing the results of those experiments.[1] This mixed tumor was found in a full-grown rat. The

FIG. 1.



tumor, which was hanging from the neck, was about 7 centimetres long, and measured from 4 to 5 centimetres in the other dimensions. This tumor hung so far from the neck of the rat that it touched the ground. It felt solid and moderately hard. About 2 centimetres from the neck, on the pendant portion of the tumor, there was a constriction encircling it and dividing it superficially into two lobes. During the operation the tumor was found to contain a small central cavity filled with straw-colored fluid. The color of the tumor in this region was white. Besides the small central cavity no cysts were macroscopically present. In trying to enucleate the tumor at the neck it was found that it had surrounded important bloodvessels and nerves of the neck, and this

[1] Further Investigation in Transplantation of Tumors. Journal of Medical Research, vol. viii.

fact prevented the possibility of saving the life of the rat. At this time it was observed that the tumor had a somewhat different color at the upper part near the neck, above the constriction; but no special

FIG. 2.

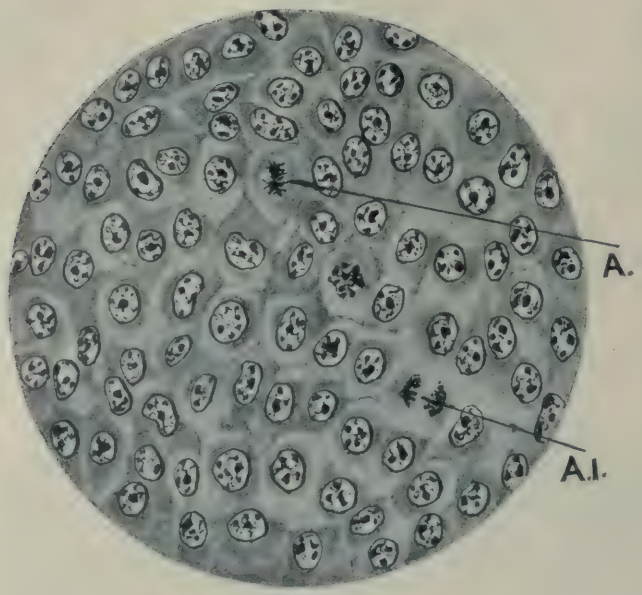
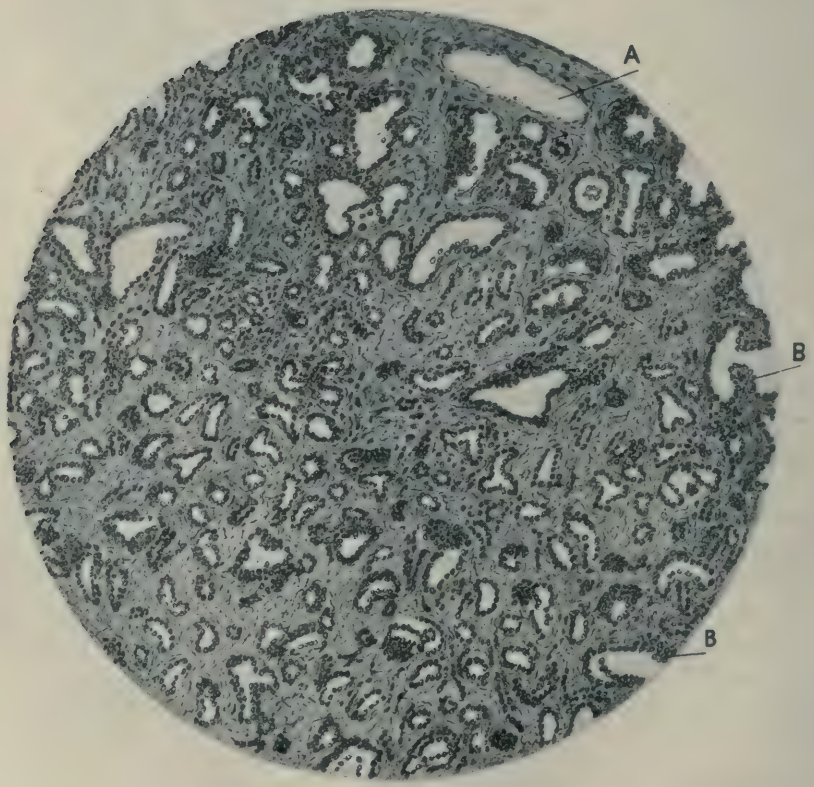


FIG. 3.



significance was attributed to this fact, and no pieces from this upper part were transplanted. Later on microscopic examination showed that the part near the neck (probably the part above the constriction) was adenocarcinomatous, but that the main mass of the tumor, which was white in appearance, was a sarcoma. In one lung a small nodule was found which showed sarcoma-like tissue around a bloodvessel, with mitoses in each section. It is very probable that we have here a beginning metastasis of the sarcomatous part of the mixed tumor of the thyroid. Further microscopic examination of the main tumor showed that the sarcomatous part consisted of spindle cells with, at different places, a somewhat varying amount of intercellular substance. The sarcomatous character was well marked, and at many places

FIG. 4.



mitoses could be seen. At other places some degenerative changes had taken place, the nuclei and cytoplasm disappearing and fibrous stroma only remaining. At such places the cells were frequently well preserved around the bloodvessels, which were thus surrounded by a mantle of cells. There was very little myxoid change present. At some places, however, small areas of softening could be seen. The epithelial part of the tumor consisted of irregularly arranged glandular structures lined with cylindrical or cuboidal cells separated by a stroma moderately rich in cells. At some places two rows of epithelial cells lined the tubules. At many places the connective tissue pushed apparently the gland cells into the tubules, so that an intracanalicular

adenomatous growth resulted. At such places the epithelium frequently became quite flat. The intruding connective tissue was often homogeneous, apparently gelatinous, and stained strongly with eosin. At other places the tubules grew in different directions through the connective tissue, so that little of the latter remained distinguishable. At the margin of some pieces the gland cells filled the alveoli—at least the appearance of alveoli filled with epithelial cells presented itself. The connective tissue surrounded by the tumor cells became necrotic, and then the epithelial masses grew diffusely as a carcinomatous growth into the surrounding tissue. There is no doubt about the malignant character of both the constituent parts of this mixed tumor. The sarcoma made a small metastasis in the lung, and it was continuously growing (mitoses); it was transplanted in a number of generations into other rats. It preserved its sarcomatous character during these transplantations, made contact metastases, and in one case many metastases in the peritoneal cavity. These metastases were always of the same type. The epithelial part had morphologically in some parts the character of a carcinoma, and also proved clinically its malignant character by growing through and destroying the surrounding tissue.

It is difficult to determine from which part of the glandular structures found in the rat in the neighborhood of the larynx the adenocarcinomatous part was derived. We can distinguish there in the normal rat at least four distinct parts, differing in their structure. In one of these only is colloid substance found. In the adenocarcinomatous part of the mixed tumor no colloid inside the tubules was found. We must leave it undecided from which of the different structures around the trachea in the region of the thyroid it was derived.

In this case the large part and the one at the distal end of the tumor were formed by the sarcoma; the smaller one and the one lying on the proximal side of the tumor was formed by the adenocarcinomatous structure. That makes it probable (although not certain) that the sarcomatous part was the one growing first, and that the adenocarcinomatous part began to grow only secondarily. In this connection it might be of interest to state that two other rats from which tumors were obtained for transplanting into rats were only affected by sarcomatous growth in the region of the thyroid. In the case reported here this sarcomatous growth seems to have been followed by an epithelial one.

Besides these four cases there have been reported by Förster, in 1860, two tumors of the thyroid gland, which he described as mixed sarcoma-carcinomata. One of these tumors had metastases in the lymph glands and in the lung. According to Förster, the main tumor consisted of mixed carcinomatous and sarcomatous parts. It affected the whole thyroid. In one jugular lymph gland sarcoma only was found. In a substernal metastasis carcinomatous structures only are said to have been present. In a second case, a man, aged fifty-eight years, this

mixed growth is said to have started in one lobe of the thyroid, which at that time already had been changed into a struma. A metastasis in the manubrium sterni was pure sarcoma. Although it is quite likely that one or both of these tumors were mixed sarcoma and carcinoma, the description is not sufficient to make it certain.

We see from the cases just described that there exist in the thyroid gland a distinct variety of mixed tumors, namely, carcinosarcomata. Although, as we shall see later, one or two similar carcinosarcomata have been described at other places, the thyroid is the only place where such a series of cases of this type of mixed tumor has been described. A certain resemblance to these tumors can be found in some of the mixed tumors of the kidney. There also we find a growth of what appear to be sarcomatous elements and of glandular structures. Metastases have been found from such tumors which contained both the sarcomatous and the glandular elements; so, *e. g.*, a metastasis in the skin, in the case of Vogler. These cases are, however, different from the mixed tumors in the thyroid gland, inasmuch as they are probably always congenital, that the gland structures do not become typically carcinomatous, and that the distribution between the epithelial and apparently connective tissue structures is a different one. The relation of the small round cells surrounding the glandular structures and the latter is interpreted in a different way by different observers. In the mixed tumors of the kidney we usually find a more or less intimate mixture between these two elements; in the mixed tumors of the thyroid it is different. In the cases reported above we find a sarcomatous and a carcinomatous part separated. In Cases I., III., and IV. we find only a small zone in which both carcinomatous and sarcomatous elements are mixed; in Case II. this zone is somewhat larger; still both constituents are in the main separated; in Cases II., III., and IV., and probably also in the two cases of Förster, metastases were present which contained one or the other of the two parts of the tumor; in Case III., also, some mixed metastases were found. In no case were such elements present which, as Wilms believes, can always be found in mixed tumors, namely, growing indifferent cells, which at the same time at the margin of the tumor multiply without any differentiation taking place, and which in the more central parts of the tumor differentiate and give rise to the same tissues which they would have produced under normal conditions in the embryo.

Another question of interest is as to the age at which these tumors occurred. In Case I. the patient was aged sixty-seven years, in Case II. fifty-five years; in Case III. the dog was twelve years old, and in Case IV. the rat was full grown; in Förster's two cases the patients were aged thirty-nine and fifty-eight years, respectively. We see that the tumors were found in patients or animals of advanced age, and

none in quite young individuals. According to the statistics of Morf, sarcoma of the thyroid is also mainly found among older people.

If we now consider the question of the etiology of these tumors we must ask if they can be explained as due to a disturbance of the embryonic development, which, according to Wilms, is at least one of the necessary conditions for all mixed tumors and also for sarcomata, even if they should be found in advanced age. As we saw, none of these tumors occurred soon after birth; almost all were found in advanced age. None of them shows the characteristic embryonic cell from which the other cells are derived by differentiation; the majority of the metastases show only one tissue. None of the conditions proving, according to Wilms, the embryonic origin of mixed tumors is to be found here. It is, however, well known that carcinoma, as well as sarcoma of the thyroid, is frequently preceded by a struma. In Cases I. and II., and in one case of Förster's, the history points to a struma preceding these mixed tumors. In the two cases observed in animals it is, of course, improbable that a slight preceding enlargement of the thyroid would have been noticed. Struma is an endemic disease caused by some condition, thus far unknown, connected with certain localities. This same condition is directly or indirectly in many cases also one of the causes of malignant tumor formation in the thyroid and, as we see also, of these mixed tumors. There exists, therefore, at present, no reason to connect these mixed tumors with irregularities of embryonic development. The widely accepted view that *all* mixed tumors must be explained as due to abnormalities of embryonic development does not, therefore, seem to be sufficiently sustained by facts.

We now have to consider the further question why we find in the mixed tumors of the thyroid gland the combination of sarcoma and carcinoma. Such combinations outside of the thyroid seem to be very rare. I have found one case described by Klein, and one other case reported by Lubarsch, which should in all probability be regarded as sarcocarcinoma.

Case I. — Klein, "Pathologisch-histologische Studie über eine seltene Combination von Sarcom und Carcinom der Nasenhöhle," Dissertation, Würzburg, 1898. This tumor was observed in a woman, aged thirty-four years. After previous bleeding from the nose in 1893 polypi appeared in the left half of the nose. In 1894 the left nasal cavity became entirely occluded. In the beginning of 1895 the left nasal cavity and the nasopharynx were filled with soft tumor masses. They seemed to originate from the base and the posterior part of the nose, and they broke through into the orbita, the oral cavity, and into the alveolar cavity of an extracted tooth. A part of this tumor consisted of an angiosarcoma, with large cells and giant cells. It penetrated, as a round-celled sarcoma, the cartilaginous septum. Pieces from the tumor near the osseous septum showed a carcinomatous character. The epithelium of the osseous septum and of the floor of the

nose was changed into thick, stratified epithelium. Carcinomatous cells penetrated into the Haversian canals.

Case II.—Lubarsch describes a tumor ("Zur Lehre von den Geschwülsten und Infectionskrankheiten," Wiesbaden, 1899) which he found in the liver of a man, aged seventy-six years. There were adenomatous and carcinomatous parts present. Between the carcinomatous structures masses of connective tissue elements were found which resembled very much sarcomatous cells. The cells were polymorphous and the nuclei hyperchromatic. Some of the tumor nodules consisted almost entirely of sarcomatous structures. The metastases consisted partially of adenomatous and partially of sarcomatous structures, including perhaps some remains of epithelial elements, and, lastly, of carcinomatous nodules, which contained in the periphery much connective tissue. A small metastasis in the serosa of the intestines consisted almost exclusively of sarcomatous cells. Lubarsch believes this tumor to be a true sarcocarcinoma.

The case of Klein resembles the sarcocarcinomata of the thyroid also in this respect, that the sarcomatous and carcinomatous parts were probably mixed only in a small zone. In the case of Lubarsch the relation between the two elements seems to have been a more intimate one. It therefore appears that outside of the thyroid only very few sarcocarcinomata have been reported. Is it entirely accidental that the majority occurs in the thyroid? That is probably not the case. Two facts might be cited which speak against this view: 1. In Cases I. and II., and in one case of Förster's, both the sarcoma and carcinoma affected the same lobe; in the other cases this may also have been the case in the beginning. The tumors were, however, too large when examined to permit a definite opinion about this point. In all cases, however, the two constituents adjoined and penetrated each other to a slight degree only. These facts speak in favor of the view that they originated in the same part and not in different parts of the thyroid. If we had to deal with an accidental occurrence in the majority of these tumors the two constituent parts ought to have started in different parts. 2. The thyroid is distinguished from many other parts of the body by the fact that sarcomata and carcinomata originate there under similar conditions. Frequently in other organs sarcomata are found in young, carcinomata in old persons. In the thyroid sarcomata and carcinomata both are mainly found in older people. Further, the predisposing conditions for sarcoma and carcinoma, as far as they are known, are usually not identical in other parts of the body. In the tongue, *e. g.*, leucoplakia frequently precedes carcinoma. It is not known, however, that leucoplakia favors also sarcoma in the tongue. In the thyroid gland, however, both carcinoma and sarcoma occur in the majority of cases in thyroids previously affected by struma. Further, carcinoma and sarcoma are the most frequent tumors of the thyroid. These facts might help to explain the relative frequency of this com-

bination of tumors in the thyroid gland, which is the more remarkable as the simultaneous occurrence of sarcoma (or endothelioma) and carcinoma even in different parts of the body seems to be rare. Wells collected seventeen cases of this kind. The occurrence of multiple simultaneous carcinoma seems much more frequent. I have observed three double carcinomata in cattle, in which carcinoma is relatively rare.[1] If we consider the great rarity of the combination of sarcoma and carcinoma elsewhere, I think it probable that there are still other factors present which cause the simultaneous growth of carcinoma and sarcoma from the same part of the thyroid. Nothing about the character of these factors can be stated until our knowledge of the causes of tumors in general is more definite. It is also remarkable that this same combination of sarcoma and carcinoma of the thyroid occurs in three different species of animals.

Besides the mixture of carcinoma and sarcoma there have been reported two sarcomata of the thyroid in which bone was mixed with the sarcomatous tissue. 1. Förster reported in a woman, aged sixty years, a sarcoma of the right lobe of the thyroid. In the centre of the tumor true bone was found surrounded by somewhat denser fibrous tissue. The bone seemed to be growing. 2. Pick found in a spindle-celled sarcoma of the left lobe of the thyroid, in a woman aged fifty-one years, bone mixed with sarcomatous tissue. The bone seemed to be growing; osteoblasts were found. At other places parts of the sarcoma assumed gradually the appearance of a tissue poorer in cells, resembling finally osteoid tissue. Similar conditions were present in a metastasis in the lung; other metastases, however, were free from bone. In this case the bone seemed to be formed directly through transformation of sarcomatous tissue. The sarcoma cells preserved their character also in the metastasis.

If we assume, with Wilms, that the sarcoma cells in this case are really not cells of connective tissue of the adult thyroid, but correspond to embryonic cells which undergo partially a further development to bone, we would have to regard these tumors, too, as true mixed tumors, best to be explained by the theory of a disturbance of embryonic development. Against this explanation speaks the fact that bone formation has also been found in struma. (Lücke, Kahn.) It is quite likely that in the case of Förster, cited above, the bone was originally formed in a struma, and that the development of sarcoma was only secondary.

We have no reason to believe that the bone formation in a sarcomatous thyroid must have a cause different from the bone formation

[1] Carcinoma in Cattle, Medicine, 1900. Besides the two cases mentioned here, I observed one case in which both kidneys were affected.

in a struma, especially since a struma so frequently precedes a malignant tumor of the thyroid. There is, however, just as little reason to believe that the bone formation in a struma is caused by irregularities of embryonic development as it would be in the case of bone formation in the valves of the heart or tuberculous foci of the lung.

All these facts and considerations do not exclude the theory that some developmental abnormalities might, nevertheless, have been the cause of the origin of both these kinds of tumors of the thyroid; they prove, however, that the causes adduced to demonstrate such an origin for other mixed tumors cannot be applied to the mixed tumors of the thyroid, and that therefore the fact that a tumor contains, besides the ordinary stroma, more than one constituent, is in itself not sufficient to prove its embryonic origin.

SUMMARY. 1. In the thyroid gland there have been found in man and in different species of animals mixed tumors of the type of carcinosarcoma. All the tumors described so far have certain characteristic points in common. Although carcinosarcomata occur in other places, the majority of them have been found in the thyroid. There also are found in the thyroid gland combinations of new-formed bone and sarcoma. *The facts which have been cited in favor of the embryonic origin of mixed tumors cannot be applied in the case of these mixed tumors. The fact that the tumor is a mixed tumor, therefore, is in itself not sufficient to prove its embryonic origin.* 2. It is not possible to determine with certainty, from the character of the constituent parts of a mixed tumor, from what kind of embryonic cells such a tumor is derived. Heterotopic tumor formations need not necessarily be produced by displaced blastomeres.

NOTE.—Recently T. McCrae (New York Medical Journal, 1902, No. 15) published a case in which the upper part of the left lobe of the thyroid of a female patient, aged sixty-nine years, was enlarged and replaced by an adenomatous new-growth; the lower part presented the structure of a round-celled sarcoma. Metastases of the sarcomatous part were found in the chain of lymph glands extending from the thyroid to the stomach and also in the right lung. The stomach was the seat of a similar sarcoma. Considering the fact that no other abdominal tumors were present, that the same lobe of the thyroid was affected by both tumors, and that the connection between the two neoplasms in the left lobe of the thyroid was the same as in some of the tumors just described, it seems not unlikely that Dr. McCrae's case, which Dr. McCrae himself regards as a primary sarcoma of the stomach, is also one to be classed among the mixed tumors of the thyroid.

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THE PATHOLOGY OF LABIAL AND NASAL HERPES AND OF HERPES OF THE BODY OCCURRING IN ACUTE CROUPOUS PNEUMONIA, AND THEIR RELATION TO THE SO-CALLED HERPES ZOSTER.[1]

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Our knowledge of herpes zoster was very much extended by the recent contribution of Head and Carpenter.[2] These authors showed, among other things: 1. That herpes zoster (in 18 cases, at least) is associated with destructive, and usually inflammatory, changes in the sensory ganglia (posterior root or Gasserian) corresponding to the nerve supply of the part affected with herpes. 2. That in recent cases (before the eleventh day) degenerative changes are not demonstrable in either the peripheral nerves, the posterior root fibres, or the central nervous system. 3. That in cases examined after the lapse of this period degenerative changes are present in these structures and apparently correspond to the affected areas in the ganglia. Their work was based upon the study of 21 cases in all stages of the eruption. They state that before their own work there were only two well-reported autopsies on cases of herpes ophthalmicus (Wys and Sattler) and five satisfactory reports on zoster of the trunk (Lesser, Chandelux and Dubler). Von Bärensprung's oft-quoted case is classified as unsatisfactory, because, though he noted the occurrence of hemorrhage into a ganglion, he failed to mention to which of the three ganglia removed he alluded.

While this valuable communication has placed our knowledge of herpes zoster on a substantial basis, it is clear that more light is needed

[1] Read at the Seventeenth Annual Meeting of the Association of American Physicians, held in Washington, D. C., 1902.

[2] Brain, Autumn, 1900.

upon the etiological factors concerned, as well as upon the identification and classification of the various types of herpes.

In order to clearly understand our present knowledge on the subject, the following summary of the main facts may be helpful. There are a number of clinical and apparently several anatomical types of herpes: herpes zoster involving the neck, trunk, and extremities (following the distribution of the spinal posterior root ganglia); herpes ophthalmicus (following the distribution of the first division of the fifth or trigeminal nerve, Gasserian ganglion); herpes facialis, herpes labialis et nasalis (probably following the distribution of the second and third divisions of the trigeminal nerve, but unsupported at this time by anatomical observations), and herpes genitalis (commonly believed to be due to local irritation and not known to be associated with any lesion of the nervous system).

The herpes facialis, labialis, nasalis, and genitalis are classed by Hartzell[1] as herpes simplex, in contradistinction to herpes zoster of the neck, trunk, extremities, and ophthalmic area (herpes zoster ophthalmicus). These latter forms of herpes have been shown to be identical in that they are associated with the same lesions of the nervous system (especially those of the sensory ganglion), and the changes in the skin are believed to be the same.

It seems further to have been conclusively demonstrated that the lesions of the skin are secondary to the primary changes in the corresponding sensory ganglia, which in turn may be brought about by a variety of causes. The cases, however, may be classified into the primary or spontaneous herpes zoster, in which the affection is apparently primary and not due to any evident preceding infection or injury, and the secondary form, in which there is more or less clear evidence that the disease occurs as the sequel or complication of some antecedent affection, as pneumonia, cerebro-spinal meningitis, etc., or to injury.

Our knowledge of the changes in the skin in the various clinical forms of herpes is far from satisfactory. Not until a sufficient number of careful observations upon the histological changes in all the stages of each variety of herpes is available will we be in a position to compare critically the processes, and, perhaps, distinguish clearly the different forms. Suffice it to say for the present, that after comparing the histological appearances described by various authors of the changes in herpes zoster, herpes labialis and genitalis (all available), with some of my own cases herewith reported, and making due allowances for the different stages of the processes studied, I am not able to find any constant distinguishing characters by which the skin lesions of the various clinical forms of herpes may be separated.

[1] Reference Handbook of the Medical Sciences, 1902, vol. iv.

I have recently had the opportunity of studying two cases which throw some light upon several points of importance in the pathology of herpes. The first case occurred in the private practice of my friend Dr. Edward F. Cushing, who recognized its interest and importance and obtained the autopsy. I take this opportunity of expressing my thanks to Dr. Cushing for the autopsy and for the use of the clinical history of the case. This case illustrates the causal relation between acute infections and herpes zoster, and emphasizes the identity of the lesions of the skin and nervous system in primary and secondary herpes of the trunk.

Case I. *Summary.* Bronchitis, acute croupous pneumonia of both lungs, herpes zoster of the left side, distributed on the back and side (sixth dorsal), and the abdomen (eleventh dorsal); congestion and hemorrhage into the capsular and interstitial tissue at one side of the eleventh dorsal ganglion, with slight cellular infiltration and destruction of a few ganglion cells; amylaceous and hyaloid bodies in another portion of the same ganglion. Slight chronic and acute interstitial nephritis, acute parenchymatous and interstitial hepatitis, acute splenic tumor, old pericardial adhesions, hypertrophy and dilatation of the heart; fibromyoma uteri.

Clinical History. Miss T., aged sixty-three years, had not been well for about one year. On October 10, 1901, she was taken sick with a cold in the head, which a few days later was followed by bronchitis. She then developed pneumonia of the lower lobe of the left lung. Later the whole of the left lung became consolidated. On the morning of October 24th there were the physical signs of consolidation of the lower lobe of the right lung. Coincidently with the consolidation of the lower lobe of the left lung there developed well-marked herpes zoster in the mid-dorsal region of the left side, extending from the middle line in the back to about the anterior axillary line, corresponding to Head's sixth dorsal area. During the last two days of life a similar eruption occurred on the abdomen, in the left umbilical and iliac regions (eleventh dorsal area; see autopsy protocol). Albumin was present in the urine. Death took place at 2.30 P.M., October 24, 1901. Autopsy six hours later. The autopsy was done hurriedly and under difficulties, at the home of the patient. The body measured 160 cm. long, was sparely built, except over the abdomen and lower portion of the back, where there was a considerable amount of fat. The body was cold, rigor mortis moderate. There were a few reddish discolored areas on the outer aspects of the legs. On the left side of the abdomen, situated in the outer and lower portion of the left umbilical and the upper portion of the left iliac regions there was an area, the size of the palm of the hand, studded with scattered pale-red or gray areas from 3 to 6 or 10 mm. in diameter. Some of these areas were elevated and covered with dry grayish-red material, while others showed a distinct loss of epidermis. No typical vesicles containing fluid were to be found, but the areas had the appearance of dried vesicles. In distribution this area corresponded with Head's eleventh dorsal area. A similar but narrow area extended from the middle line in the mid-dorsal region as far as the anterior axillary line under the nipple,

corresponding to Head's sixth dorsal area. The areas here were larger and the process appeared older than that on the abdomen. No other lesions were found upon the surface of the body. There was no facial herpes.

Chest. The chest was fairly well shaped, the muscles and fat rather wasted.

Both pleuræ were free from adhesions, and the pleural cavities contained no fluid. The visceral pleuræ over considerable areas were covered with a thin layer of fibrin, and were red and lustreless.

Right Lung. The apex was free from puckering and thickening. The upper lobe on section was congested and markedly œdematous. The whole of the middle and a large part of the lower lobe were consolidated, airless, and of a grayish-red color, and granular appearance. The mucous membrane of the bronchi was congested.

Left Lung. The whole lung was consolidated, airless, of a gray or grayish-red color, and granular appearance. The bronchial mucosa was congested. The bronchial glands were pigmented, but free from tubercle.

Heart. The pericardium was adherent to the diaphragm over a large area. Firm fibrous adhesions obliterated the pericardial sac. The walls of both ventricles were thickened. The valves, the coronary arteries and veins, as well as the aorta and large arteries, were normal. The myocardium was pale, otherwise normal; the heart weighed 400 grammes.

Abdomen. The muscles and fat of the abdominal wall were of ordinary appearance. The left lumbar region was prominent. The stomach was distended with gas, the large and small intestines contracted.

Liver. The liver was of ordinary appearance and size. The edges were rounded, the surfaces smooth, consistency not increased. On section the lobules are visible, the surface pale. The gall-bladder and bile-ducts were negative.

Spleen. The spleen was twice the ordinary size. On section it was of a grayish-red color; the trabeculæ and Malpighian bodies visible; consistency decreased.

Kidneys. The kidneys were of about the same size and appearance. The capsules were adherent in places, the surfaces were somewhat granular and marked by a few old scars. On section the consistency was somewhat increased, the surfaces pale, the cortices thinner than ordinary. The arteries, pelvis, ureters, bladder, and adrenals appeared normal, as did the stomach and intestines.

The ovaries were small and tough to the touch. The uterus was considerably enlarged; the body was the seat of a globular fibroma the size of an orange.

Nervous System. The brain could not be examined, and the examination was confined to the lower portion of the spinal cord; from the tenth dorsal segment downward with the cord the eleventh and twelfth dorsal and first lumbar posterior ganglia of both sides were removed. It was not possible to go higher in the time available for the examination. There was an excess of cerebro-spinal fluid, which, however, was quite clear. The meninges were normal in appearance. The cord showed no lesions on section. The ganglia showed no macroscopic lesions, and no hemorrhages were found about the posterior roots or the nerves going from the ganglia.

Portions of the various organs, including the cord and the ganglia, were hardened in Orth's fluid. The ganglia were transferred to 96 per cent. alcohol after a few hours. Portions of various organs, including the skin, were also hardened in Zenker's fluid.

Bacteriological Examination. Cover-slip preparations from the lungs and pleuræ showed lanceolate diplococci in capsules. Cultures on blood serum and on glycerin agar from the lungs, heart's blood, liver, spleen, kidneys, and cerebro-spinal fluid remained sterile.

Histological Examination. Lungs. Sections from both lungs showed well-marked croupous pneumonia, with lanceolate diplococci in the alveolar exudate.

Liver. There was well-marked fatty degeneration of the liver cells, congestion of the capillaries, with marked round-cell infiltration about many of the portal systems. No focal necrosis and no bacteria were found in suitably stained sections.

Kidneys. There were scattered areas of chronic glomerulitis, with thickening of the capillaries and of Bowman's capsule, with but little atrophy of the neighboring tubules. The epithelial cells of the convoluted tubules showed cloudy swelling. With no apparent relation with changes in the glomeruli or tubules, there were numerous areas of round-cell infiltration; most of these cells were of the plasma-cell type, but some were lymphocytes. There was no necrosis of the renal epithelium and no abscess formation. No bacteria were to be found.

Skin. Sections were made through both areas of herpes, and, with the exception that the lesions were more extensive in the older lesion (sixth dorsal region), the changes were the same. There were few unbroken vesicles, but in most places the surface of the lesion was covered with amorphous and fibrillated fibrin containing a larger or smaller number of desquamated, swollen, and often disintegrating and necrotic epithelial cells. Some of these cells had undergone coagulation, and others liquefactive necrosis. In some places the cells of the deeper layer of the epidermis were markedly swollen, vacuolated, and evidently dropsical. In the fibrin and among the epithelial cells on the surface there were variable, often great, numbers of polymorphonuclear neutrophilic leucocytes. In some places there were cavities formed by the elevation of the superficial or subcorneal layer of epithelium. These were of considerable size in places, but were not numerous. Other small vesicles occurred in the exudate, their walls being formed by necrotic cells. Still other vesicles were between the epidermis and the underlying papillary layer. These were always small. In many places the papillary layer was exposed by the total destruction of the epidermis, and was covered by the exudation. In the papillæ and in the upper layer of the corium the veins and capillaries were markedly dilated, and in places there was hemorrhage, either into the tissue or upon the surface.

The papillæ and the upper layers of the corium showed other intense changes, coagulation necrosis, with hyaline and fibrinoid changes, nuclear fragmentation, and infiltration, with large numbers of polymorphonuclear neutrophiles, lymphocytes, and some plasma cells. Here and there a few eosinophiles were to be seen. This cellular infiltration was both diffuse and along the bloodvessels. Many of the sweat glands and hair follicles were swollen and distended with leucocytic and serous exudate. The epithelial cells were commonly swollen,

granular, and often desquamated and necrotic. About many of these glands there was well-marked leucocytic infiltration, a few of the cells being eosinophiles. Scattered collections of leucocytes were also seen in the deeper layers of the skin. No bacteria were to be found in any of the lesions in sections stained by Weigert's fibrin method or with eosin and methylene blue.

The whole appearance of the lesion points to rapidly necrotic and exudative processes.

Posterior Root Ganglia. Sections were cut of the eleventh and twelfth dorsal and first lumbar ganglia of both sides and stained by Nissl's, Weigert's, and Marchi's methods, as well as with methylene blue and eosin, and hæmatoxylin and eosin. Sections from all the ganglia studied, except the eleventh dorsal of the left side, were entirely normal.

In sections of the latter ganglion changes were found in two places: (1) at one side of the ganglion about midway of its length, and (2) at the peripheral end.

1. In the sections cut transversely through about the middle of the ganglion at one side there was considerable hemorrhage, with pigmentation, into the capsule. In some of the sections corresponding to the area of capsular hemorrhage there was just beneath the capsule marked congestion of the capillaries and interstitial hemorrhage between the ganglion cells. In several sections small areas of cellular infiltration about destroyed ganglion cells were found. The ganglion cells elsewhere stained well and appeared normal.

2. At the peripheral end of the ganglion there were a number of amylaceous and hyaloid bodies, both singly and in groups, of the size and shape of ganglion cells, and lying in spaces similar to ganglion cell spaces. Many of these bodies were finely granular, some of the granules staining pink with eosin, and others blue with toluidin blue. Many bodies stained diffusely pink with eosin, and some diffusely blue with blue dyes. In some a central nucleus was apparent, and many showed a concentric arrangement. In a few places hyaline masses were made out in lymph spaces and in blood capillaries. Hyaloid and amylaceous bodies were also found in unmistakable lymph and blood-vessels. The question whether or not some at least of these bodies represented degenerated nerve cells is difficult to answer. From careful study I am convinced that some of them were formed and lie in nerve cell spaces. No lesions of the peripheral nerve, the posterior nerve roots, or in the spinal cord, could be made out.

The interpretation of the pathological changes of the above case appear to be as follows:

Acute croupous pneumonia following bronchitis, with the ordinary parenchymatous changes of the liver and kidneys common in such cases, with the addition of acute interstitial hepatitis and nephritis; an herpetic eruption of certain cutaneous areas, the spinal root ganglion corresponding to one of which areas was shown to be the seat of definite lesions (congestion and hemorrhage of both the capsule and a small area of the interstitial tissue of the ganglion, with cellular infiltration about a few degenerated ganglion cells, with hyaloid and amylaceous bodies, in another portion of the ganglion).

It seems fair, in the light of our present knowledge, to attribute these various lesions to the toxins of the pneumococcus.

The failure to find degenerative changes in the cord, the posterior roots, and the peripheral nerve is in accord with observations of Head and Carpenter, who did not find changes in these organs in a case of herpes dying on the eighth day. They were present in a case dying on the thirteenth day.

Including the 5 cases of Lesser, Chandelux, and Dubler with the 16 cases of Head and Carpenter, there are 21 well-studied cases of herpes zoster of the trunk in which definite destructive lesions have been demonstrated in the posterior root ganglia, corresponding to the distribution of the herpetic eruption. Two of the 21 cases of Head and Carpenter involved the head, in 1 case the ganglion was not removed, and in 2 others, in which death took place in 139 and 240 days, respectively, no lesions of the nervous system were found. In all 9 of the acute cases (three to sixteen days after the appearance of the eruption), definite and unmistakable ganglionic lesions were found. Of these cases 2 had had acute infections (cystitis, with retention of urine in paraplegia, and acute bronchitis and tubercular pneumonia). In the 12 chronic cases in which death occurred in from 57 to 790 days after the herpes the sensory ganglia corresponding to the distribution of the eruption showed well-marked chronic changes.

Our next case shows that the changes in the skin and Gasserian ganglion in herpes of the lips and nose in pneumonia are identical with those occurring in herpes ophthalmicus, and in the skin and posterior root ganglia in both primary and secondary herpes zoster of the trunk. It is also, curiously enough, apparently the first case of herpes of this region in which changes have been sought for in the Gasserian ganglion.

Case II. *Summary.* Acute croupous pneumonia in a bartender, aged forty-one years. Death on the sixth day of the disease. Two days before death well-marked herpes of the upper lip and the nose, being much more extensive on the left side.

Autopsy showed acute croupous pneumonia (gray hepatization) involving the whole of the right lung, with fibrinopurulent pleurisy of the left side, œdema and congestion of the left lung. Chronic fibrous obliterative pleurisy of the right side. Herpes of the upper lip and nose, most marked on the left side. Congestion of the veins about the origins of the superior maxillary branches of both Gasserian ganglia. Hemorrhage into the capsule and tissue, with interstitial cellular infiltration and compression and degeneration of the ganglion cells near the origin of the superior maxillary branch of the left Gasserian ganglion. A few small areas of cellular infiltration in the same part of the right Gasserian ganglion. Marked congestion of the veins of the neck and brain and of the cerebral sinuses. Pneumococcus in the right lung and left pleura.

Clinical History. For permission to use the clinical history of the following case I am indebted to the courtesy of my colleague, Dr. J. H. Lowman, in whose service in the Lakeside Hospital the patient was admitted February 6, 1902, complaining of pain in the right side of the chest, cough, and fever.

The patient was a male, aged forty-one years, white, and a barkeeper by occupation. His family history was without present interest.

Personal History. He did not recall having ever been sick before, and denied having had diphtheria, scarlatina, rheumatism, pneumonia, pleurisy, syphilis, gonorrhœa, typhoid and malarial fevers. Some time ago he injured his right temple by a fall, but the wound healed promptly and was followed by no clinical symptoms. He drank beer and whiskey to excess at times, and also used tobacco. He had been a barkeeper for twelve years.

Present Illness. He got his feet wet on the night of February 8th, and awoke the next morning with severe pain in the right side of the chest, but did not have a chill.

On admission he had the physical signs of consolidation of the lower portion of the right lung. The left lung was clear. The spleen was enlarged. Examination of the other organs was negative. The leucocyte count on February 8th was 19,000, and on February 9th 13,000 per cubic millimetre. On February 9th, the fourth day of the disease, there appeared a well-marked vesicular eruption over the upper lip and the outer surface, and in the vestibule of the left side of the nose. This eruption on the lip and the outside of the nose extended somewhat to the right side of the median line. The sputum contained lanceolate diplococci. By February 11th the whole right lung was consolidated, and numerous moist râles were to be heard over the left lung.

The patient was delirious. Death occurred suddenly at 1.15 P.M., February 11, 1902, on the fifth day of the pneumonia and the beginning of the third day of the herpetic eruption.

Autopsy One Hour after Death. Body warm, no rigor mortis. Body 165 centimetres long, well built, and well nourished. There were no marks, scars, or wounds on the body. On the upper lip, involving both mucous and skin surfaces, there were a number of dried crusts surmounting slightly elevated areas, with red margins. These areas varied from 2 to 5 millimetres in diameter. Similar papules and dried vesicles were present on the skin of the vestibule and external surface of the left side of the nose. Altogether there were from fifteen to twenty such areas. Several similar lesions were also found to the right side of the median line of the lip and nose. No other herpetic eruptions were to be found on the body.

Nervous System. The veins of the dura and pia arachnoid and all the sinuses were markedly congested; the pia arachnoid was smooth and glistening. The structures at the base of the brain were normal. The brain on section showed congestion, but was otherwise normal in appearance.

The Gasserian Ganglia. The veins near the ganglion were engorged with blood. The ganglion was of ordinary size. On the upper surface just below the entrance of the sensory root and between and about the exit of the ophthalmic and superior maxillary branches the veins were congested and stood out prominently. The same appearance was seen on the posterior surface, but the congestion was less well marked.

The Left Ganglion. The vessels about the ganglion were engorged, as were the veins about and between the origin of the ophthalmic and superior maxillary branches of the ganglion. About the root of the superior maxillary branch this was very marked, and there was also hemorrhage into the capsule at this part on the posterior aspect of the ganglion. The fifth nerve and the branches from both ganglia appeared normal. The cord and the posterior root ganglia were not removed.

Chest. The chest was well formed; the sternum, ribs, and costal cartilages were normal.

The right lung was bound down by old but thin adhesions; the pleural cavity was obliterated. The right lung was consolidated throughout. On section it was firm and airless, of a grayish color, and quite granular in appearance. The mucosa of the bronchi was congested, otherwise normal. The left pleural cavity contained about 100 c.c. of seropurulent fluid. The surface of the lower lobe was covered with a thin fibrinous exudate. The lung crepitated throughout. On section the lung was markedly congested and œdematous, but was free from consolidation.

The description of the other organs is without present interest, and will, therefore, be omitted.

Cover-slips from the right lung and left pleura showed encapsulated lanceolate diplococci.

Plate cultures from both lungs, the left pleura, and heart's blood and pericardium showed pneumococcus in pure culture. Similar cultures from the liver, spleen, kidneys, and gall-bladder remained sterile.

Histological Examination. Lungs. Sections of the consolidated area showed well-marked croupous pneumonia, with lanceolate diplococci in the exudate. Sections of the other organs, with the exception of the skin of the lip and nose and of the Gasserian ganglia, showed nothing of present interest.

Skin of Lip and Nose. Bits of tissue were cut out and hardened in formalin and 95 per cent. alcohol, and sections were stained in carbol-toluidin blue and eosin, hæmatoxylin and eosin, and by Weigert's fibrin method.

The changes found were practically identical with those from the herpetic areas of Case I.

As in Case I., few well-developed vesicles remained, the surface of the lesions, as a rule, being covered with a crust of amorphous and fibrillated fibrin and fibrinoid material containing desquamated and often necrotic epithelial cells, polymorphonuclear and mononuclear leucocytes, and cellular and nuclear fragments. Here and there rather small vesicles could be made out. As in Case I., some were elongated cavities in the exudate, or in the superficial layer of the skin, just beneath the horny layer, while others were between the underlying inflamed papillæ and the epidermis. Most of the latter cavities were small, and their walls were formed of necrotic epithelium and their floors of the naked papillæ. In some places ballooning of the cells of the epidermis could be made out. In many places the margin between the necrotic and the unchanged epidermis was rather clear cut, but in some places near the necrotic portions the small vesicles could be made out in the neighboring otherwise normal epidermis. In most places at the site of the lesion the whole thickness of the epidermis was necrotic.

Beneath the fibrinous layer there were, in all sections examined, changes in the epithelium, marked coagulation and liquefactive necrosis, and hyaline transformation of the cells. The papillary layer and outer part of the corium were similarly affected. There was, in many places, marked nuclear fragmentation. The epithelium of the sweat glands and some of the hair follicles, when present, showed changes—swelling and liquefaction, and often a reticular appearance. Some cells were markedly swollen, many cells showed coagulation necrosis. Many nuclear fragments were to be seen. The bloodvessels, especially the capillaries and small veins of the papillæ and corium, were markedly dilated. Some were crowded with leucocytes. In some of the superficial vessels there were thrombi composed of pink-staining material. The papillæ and the superficial portions of the corium were diffusely infiltrated with great numbers of polymorphonuclear, neutrophilic, and large and small mononuclear leucocytes, and some plasma cells. The leucocytic infiltration could also be traced along some of the small vessels into the deeper layers of the corium. About some of the superficial veins and capillaries often large numbers of red blood cells had escaped into the tissue. Some of the lymph spaces were dilated. The lesions here, as in the herpes of Case I., were both degenerative and exudative, and involved both epidermis and corium. No inflammatory changes were found in nerves in the skin. No bacteria were found in the lesions of the skin, but in the superficial part of the fibrinous exudate, in sections taken from the vestibule of the nose, diplococci and some bacilli, morphologically like B. mucosus capsulatus, were found.

Gasserian Ganglia. The ganglia with the fifth nerve roots and the origins of the ganglionic branches were hardened in formalin (10 per cent. solution).

The two ganglia were mounted in celloidin, side by side, on the same block and cut in serial sections, every other section being stained and mounted in order. Many of the alternate sections were also stained.

In mounting on the block the left ganglion was at a somewhat higher level than the right, so in the parallel sections as mounted for histological study the two ganglia were not identical in structure, but as the series was followed to the end the right ganglion was found to be similar to the left in structural detail.

Left Gasserian Ganglion. In sections 1 to 8 there were no ganglion cells near the superior maxillary branch. The veins about this branch were enormously dilated and filled with red blood cells. In some places in the largest vein there were collections of leucocytes and larger and smaller granular masses, suggesting fibrin. No changes were found in the opposite end of the ganglion. About the dilated veins there was hemorrhage into the pia or capsule of the ganglion. In section 9 a small oval bit of ganglion tissue, containing ganglion cells, became apparent near the superior maxillary branch. In sections 9, 10, 11, and 12, corresponding to this, there were capsular and subcapsular hemorrhage, with compression of the superficial ganglion cells. In sections 15 to 35 the small strip of ganglion tissue in relation with the superior maxillary branch became very much larger, and formed an elongated strip of tissue traversing the thin portion of the ganglion, reaching from the side of the superior maxillary branch to, but not

uniting with, the larger ganglionic mass corresponding to the origin of the inferior or third branch. About the middle of this strip there was marked congestion of the veins about the superior maxillary branch, into and, here and there, just beneath the capsule of the ganglion. This congestion and hemorrhage must have compressed the ganglion cells in this region. Sections 36 and 37 showed the first well-marked changes in ganglion cells and interstitial tissue. About the central portion of this strip of ganglion tissue some of the ganglion cells were vacuolated, others were very pale, non-granular, homogeneous, and stained poorly. The nuclei showed no special changes. Some ganglion cells were evidently necrotic, the cytoplasm staining diffusely, and the nuclei being displaced to one side. Here, especially about the changed ganglion cells, there was marked cellular infiltration, with plasma cells, lymphocytes, and polymorphonuclear neutrophiles.

These cells were both in the interstitial tissue and grouped about changed ganglion cells, which were evidently compressed thereby. In places there had evidently been a proliferation of the endothelial cells about the ganglion cells.

In sections 40 to 60 the congestion and hemorrhage were noticeable, the cellular infiltration being inconspicuous.

Beginning in section 73, cellular infiltration became marked again. In section 77, in the above-mentioned strip of ganglion tissue involving an area of from twenty to twenty-five ganglion cells, there was marked cellular infiltration with interstitial hemorrhage. Some of the ganglion cells were necrotic. Smaller areas of interstitial cellular infiltration were found near this area.

Section 78, showed, at the border of the same hemorrhagic area a group of degenerated ganglion cells surrounded by large numbers of lymphocytes, plasma cells, and polymorphonuclear leucocytes, red blood cells, and proliferated endothelial cells of the pericellular spaces. The ganglion cells of the affected area showed the same changes described above; many have entirely disappeared. They seemed to have been compressed and destroyed by the interstitial exudate and hemorrhage. A few ganglion cells in this area were the seat of large vacuoles. Nuclear figures could be made out here and there in the cells of the interstitial infiltration. In most of the sections from 60 to 85 these changes were more or less well marked. The area of hemorrhage could be traced in them all. The changes in the left ganglion were lost after the 95th section.

Right Gasserian Ganglion. All the sections cut showed congestion of the veins and capillaries about the second or superior maxillary branch, as described for the right ganglion. Hemorrhage was, however, absent. In sections 80 to 95 a few areas of cellular infiltration were found in the area corresponding to that showing similar changes in the left ganglion.

These areas of cellular infiltration were small and scattered, and nothing like so well marked as those found in the left ganglion. In both ganglia a considerable number of amylaceous and hyaloid bodies were found in the lymph spaces.

In preparations of the fifth nerve, and of the superior maxillary branches of both sides, made by Marchi's method, no degenerations were to be found.

No bacteria were found in the ganglia or in the dilated veins.

That herpes zoster, following some part of the distribution of the trigeminal nerve is due to changes in the Gasserian ganglion is supported by observations on four previous cases.

Wys, in 1871 (quoted by Head and Carpenter), reported a case of herpes zoster involving the distribution of the whole of the first division of the trigeminal nerve ; the patient died on the seventh day of the eruption. There were thrombosis of the ophthalmic vein, abscesses of the eye muscles, and purulent infiltration of the connective tissue of the eyeball. There was hemorrhage about the origin of the ophthalmic division and about the inner side of the ganglion. Microscopically, there was extravasation of blood into the ganglion and into the first division of the nerve, with purulent inflammation of the ganglion.

Sattler, in 1875 (quoted by Head and Carpenter), reported a case of herpes ophthalmicus of the right side, in a man, aged eighty-five years, occurring some days after carbonic oxide gas poisoning. Death occurred fourteen days afterward. In the corresponding Gasserian ganglion there was destruction of ganglion cells and small-cell infiltration. The ophthalmic branch of the nerve showed degeneration, the other branches being normal.

Head and Carpenter reported a case of herpes of the right frontal region in which, one hundred and ninety days later, at autopsy, they found hemorrhage and destruction of ganglion cells in the right Gasserian ganglion.

In another case these authors studied the right Gasserian ganglion thirty days after an attack of herpes of the chin and cheek of the right side of the face (third division). " In that portion of the right ganglion which receives the fibres of the inferior maxillary branch of the nerve " there was congestion of the bloodvessels, destruction of ganglion cells, and cellular infiltration. Degenerated fibres were found in the fifth nerve central to the ganglion, in the pons and medulla, as well as in the inferior maxillary division of the fifth nerve.

Both of the last two cases were subjects of general paralysis. Wys' case was apparently spontaneous, while that of Sattler followed carbonic oxide gas poisoning. As far as I am able to find, these comprise all the observations on the relation between changes in the Gasserian ganglia and herpes distributed along the course of the trigeminus. Of these four cases, three were examples of ophthalmic herpes, and one of inferior maxillary herpes. I am not aware that the relation of the changes in the Gasserian ganglia to herpes of the upper lip and nose, occurring either spontaneously or in the course of pneumonia, malaria, cerebro-spinal meningitis, gastro-intestinal disorders, and other infections and intoxications, has been investigated.

I wish to call attention to the practical identity of both the lesions of the skin and of the nervous system in these two cases of herpes, the

one of the trunk, and the other of the upper lip and nose, both occurring during the course of acute croupous pneumonia. Reference to the detailed descriptions will, I think, show that the lesions agree in all important particulars, and only differ in severity. The extent and severity of the skin lesions are also in definite relation to those of the corresponding ganglia. The skin and ganglion changes in Case II. (trigeminal distribution) were more severe than in Case I. (dorsal 11). One is forced to the conclusion that the herpes of the trunk and the herpes of the lip and nose occurring in these two cases are identical clinically, histologically, and probably etiologically. They further demonstrate that the ganglionic lesions of herpes zoster of the trunk and herpes of the lip and nose occurring in pneumonia are identical with those described by previous observers for herpes zoster of the trunk and extremities and herpes distributed along both the first and third divisions of the trigeminus, occurring both spontaneously (idiopathic herpes), and secondarily to acute infections, as cystitis, bronchitis, acute tubercular pneumonia (Head and Carpenter), after poisons, as carbonic oxide gas (Sattler), and the invasion of tumors (Head and Carpenter). As far as I have been able to learn, no anatomical studies have been made on the lesions of the nervous system in herpes of the lip and nose occurring in malaria and other continued fevers, in pneumonia, cerebro-spinal meningitis, coryza, or gastro-intestinal disorders. We are also without similar observations in genital herpes. In the case of the latter, however, Unna's description of the skin lesions, based on observations in three cases, is practically identical with his findings in a case of herpes labialis in an individual dead of a continued fever, with these lesions of our cases and with those found by Head and Carpenter and others in herpes zoster. Unna, however, found marked ballooning of the epithelial cells of herpes zoster (trunk?), a condition not found by him in herpes genitalis and his one case of herpes labialis.

In our case of labial and nasal herpes, in some places the swelling and liquefaction of the epithelial cells, especially in the hair follicles, was better marked than in the case of herpes of the trunk. It seems likely that in a necrotic and exudative process passing rapidly through different stages the changes would not be uniform in the lesions of each and every case. All that can be said at present is that the skin lesions of our two cases are identical and agree with those described by most authors.

Though there are no previous observations on the relation of changes in the nervous system in herpes labialis and nasalis occurring in pneumonia, and none at all in malaria, for the third acute infectious process in which herpes is common there are some most interesting and suggestive data. I refer to epidemic cerebro-spinal meningitis. In their

monograph on this disease, Councilman, Mallory, and Wright[1] call attention to the frequent occurrence of herpes of both the lips and nose, and to the fact that it may appear on other parts of the face and even elsewhere on the body; and in the summary on page 163 they state that "in its (the infection) extension along the fifth nerve it produces an acute inflammation of the Gasserian ganglion, with destruction and degeneration of the nerve cells composing it." On page 114 they state that sections were made of the Gasserian ganglia in five cases and of the spinal ganglia in two. The Gasserian ganglia in acute cases were "infiltrated with pus, and masses of ganglion cells were often separated from their connection." There was more or less hemorrhage; some ganglion cells were small and some devoid of nuclei; some cells contained large vacuolar spaces. Diplococci were found in some sections. In the more chronic cases the amount of leucocytic infiltration was less, but there was marked proliferation of the interstitial tissue, and in one case there was œdema, with marked cellular infiltration, especially about the ganglion cells, lymphoid, epithelioid, and plasma cells being found. There was atrophy, often going on to complete necrosis of the cells (ganglion cells). The spinal ganglia were not equally affected, but all seemed somewhat swollen and œdematous. On microscopic examination much the same changes were found in these as in the Gasserian ganglia. Degenerative changes were, of course, to be found in the nerves. They also showed that these changes may occur rapidly, for purulent infiltration was observed in the ganglia of a goat twelve hours after inoculation of the diplococcus intracellularis meningitidis into the spinal cord.

On page 125 they state that in one case the herpetic vesicles on the lip were examined. In them there was extensive infiltration, with pus cells in the tissue around the vessels, and proliferation of the fixed cells of the tissue. No mention is made of the epithelium; no diplococci were found in the pus cells.

Unfortunately no statement is made concerning the presence or absence of herpes of either the head or the trunk in the cases showing lesions of the Gasserian and spinal ganglia. In the one case showing skin lesions (small, dark purplish spots on the trunk and extremities) coming to autopsy they found congestion and dilatation of the blood-vessels of the skin, with hemorrhage in places, and in some places proliferation of the cells about the vessels. In the centre of the hemorrhagic area there was some infiltration with pus cells, and in one place the upper layers of the epithelium were slightly elevated by the accumulation of pus cells beneath.

These observations furnish at least ample explanation for the occur-

[1] Report of the State Board of Health of Massachusetts, 1898.

rence of herpes of both the head and trunk in meningitis. The influence of the changes in the ganglia upon the other changes in the skin are, of course, only conjectural.

Etiology of Herpes. From what has gone before, it is evident that the lesions of the skin and nervous system of primary, or idiopathic, or spontaneous herpes zoster of the head, neck, trunk, and extremities are the same, as are also the same lesions in certain cases of herpes of the trunk and face (upper lip and nose) occurring in pneumonia (Howard), and similar lesions of the nervous system in herpes of the trunk occurring in acute cystitis in a man with paraplegia, acute bronchitis; pernicious anæmia in a patient who had taken arsenic, and after the invasion of a lymphosarcoma (Head and Carpenter), and finally in ophthalmic herpes after poisoning with carbonic oxide gas (Sattler).

Primary herpes zoster is regarded by Head and Carpenter, and by Van Harlingen[1] and others, as an acute specific infectious disease due to an unknown cause, having a selective affinity for certain sensory ganglia in which certain degenerative, destructive and often inflammatory lesions are produced. These lesions in some unknown way cause acute degenerative, exudative, and proliferative changes in the skin and mucous, and possibly serous, membranes corresponding to the nerve distribution of the affected ganglia. There is a considerable amount of evidence in favor of the hypothesis that there is an acute specific infectious process of this nature, but no convincing proof has been so far adduced in its support.

It must be further borne in mind that there is a large group of cases of herpes either following the action of known toxins (carbonic oxide gas and arsenic), the involvement of the ganglia by tumors, or occurring in the course of certain infections, as pneumonia, malarial and typhoid fevers, and cerebro-spinal meningitis (in which, as has been shown, there are often intense lesions of the sensory ganglia), in all of which the lesions, as far as is known, are identical. Herpes, like pneumonia, meningitis, and inflammation in general, is a pathological condition, with definite lesions, capable, however, of being excited by a variety of causes, and is not always produced by the same causes; an efficient cause being one producing compression, degeneration, or destruction of ganglion tissue. It is not improbable that the primary lesions are often due directly or indirectly to the soluble toxins of various micro-organisms. The special frequency of labial and nasal herpes, and of herpes of the head and face in general, in malaria, pneumonia, and cerebro-spinal meningitis, is readily explained. In the case of malaria the organisms in the circulating blood often accumulate in the brain, where the Gasserian ganglia may be readily affected by con-

[1] The American Journal of the Medical Sciences, January, 1902.

gestion, the action of toxines, or even by capillary thrombi of parasites. In pneumonia, the organisms or their toxines may locate in the ganglia. What, however, to my mind seems the most reasonable predisposing cause of the frequent occurrence of labial and nasal herpes in this disease is the marked passive congestion which is so often present. This was especially noticeable in Case II., in which there was marked congestion of not only the bloodvessels and sinuses of the brain and meninges, but of the vessels of and near the Gasserian ganglia themselves, and especially about the second division. This marked congestion, which favors hemorrhage, the action of the toxines, poisons, and organisms in the blood, and thrombosis, may probably of itself, by pressure and by interfering with nutrition of the ganglion cells, cause degeneration sufficient to excite the herpetic changes.

As Councilman, Mallory, and Wright have shown, in epidemic cerebro-spinal meningitis, the spinal sensory ganglia, and especially the Gasserian ganglia, are often the seat of extensive changes due to the extension of the infection along nerve sheaths to these ganglia.

There is, *a priori*, no reason why changes in these ganglia should not occur in bronchitis and pleurisy. There is also no reason why the peripheral lesion in herpes zoster should not affect the pleura, as suggested by Curtin, just as the same process is known to affect the mouth, cheek, and pharynx. We know nothing in regard to the relation of lesions of the nervous system to the so-called simple herpes (with which labial and nasal herpes of pneumonia, malaria, and epidemic cerebro-spinal meningitis have hitherto been included) of the face, especially of the lips and nose, occurring in coryza, gastro-intestinal disorders, and the herpes genitalis.

It is to be hoped that observations will be made on this point, and it is not impossible that some cases, at least, will fall in the class we have been considering.

The question why should the peripheral changes occur after the lesions of the nervous system found in herpes is a difficult one to answer. There is no evidence that the skin lesions are due to the local presence of parasites, infection with which is predisposed by the nerve lesions.

Head and Carpenter are "inclined to think that the trophic disturbances of the skin are an extreme form of activity of the same cells, disturbance of which by afferent impulses along the white ramus produces the hyperalgesia that accompanies visceral referred pain;" but they "do not imagine that the eruption of herpes zoster is produced by disturbance of special trophic nerves, but by intense irritation of cells in the ganglion which normally subserves the function of pain, and more particularly that form of pain produced by afferent visceral impulses."

This is, however, far from explaining why irritation of these ganglion cells and nerve fibres causes a severe inflammatory process marked by intense vascular changes, cell destruction, exudation, and proliferation. The presence of hyaline, granular, and apparently red blood cell thrombi in many of the dilated bloodvessels of the herpetic areas in my cases is of interest, and may account for the hemorrhage, but were hardly extensive enough to explain the necrosis. What was the origin of these thrombi? Were they associated with changes in the vascular endothelium due to nerve changes? Were the hemorrhage and exudation due, in part, to the increased permeability of the vessel walls, the result of loss of nerve control or nerve irritability? These are some of the questions awaiting solution.

Conclusions. 1. Herpes zoster is a pathological condition, like pneumonia, for instance, with definite lesions of certain sensory ganglia, sensory nerves, and the skin, capable of being excited by a variety of causes. It is probable that the primary ganglionic lesions are commonly due directly or indirectly to the soluble toxines of various micro-organisms. The skin lesions may be on the head, neck, trunk, or extremities, corresponding to the Gasserian and posterior root ganglia affected.

2. Various forms can be distinguished. *a.* Spontaneous or primary herpes, thought by Head and Carpenter, and others, to be a specific infectious disease, the specific causal agent of which has a special affinity for certain sensory ganglia (posterior spinal and Gasserian). *b.* Herpes occurring after certain definite toxic agents, as arsenic and carbonic oxide gas, etc. *c.* Herpes occurring in the course of certain acute infectious diseases, as pneumonia, cerebro-spinal meningitis, and probably of malarial and typhoid fevers. The lesions of the ganglia and of the skin in the above three forms are the same, and the processes, therefore, presumably identical. *d.* Herpes simplex, so-called, affecting the lips and nose in coryza, gastro-intestinal intoxications, etc., and genitals (herpes genitalis) has not been sufficiently investigated to be classified; no evidence exists for or against its connection with changes in the nervous system.

3. As far as changes in the skin in herpes are concerned, they are illustrations of particular forms of necrosis and inflammatory reaction, and, as in similar lesions in other organs, can probably be excited in a variety of ways.

4. Herpes should be classified according to its relation to changes in the nervous system, and to this end every possible opportunity should be embraced for extending our knowledge in this direction.

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AN EXPERIMENTAL STUDY OF LITHIUM.*

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Lithia was discovered by Arfwedson, in 1817, in the mineral petalite. Since that time lithium has been shown to be widely distributed in nature, but occurring only in small quantities. It occurs in various minerals, in mineral waters, in sea water, in the ash of plants, and in some vegetables used as foods. It has also been found in the ashes of blood and milk. It always occurs in combination as an oxide, chloride, silicate, or fluoride, with potassium and aluminum. Lithium belongs to the group of alkalies and has an atomic weight of only 7 +.

Lithium seems to have been first introduced into medicine by Sir Alfred Garrod[1] about the year 1863, for the cure of gout and rheumatic gout. The reason for its introduction was that lithium was found to be an excellent solvent for uric acid and the urates in experiments, and it was supposed that by giving the substance the deposits in and around the joints could be disposed of and further deposits prevented. Lipowitz,[2] in 1841, was one of the first to show the marked affinity of lithium salts for uric acid, showing that it formed an acid salt soluble in sixty parts of water at 122° F. In 1843 Dr. Alex. Ure[3] found that a urinary calculus composed of alternate layers of uric acid and oxalate of lime when placed in a solution of 4 grains of lithium carbonate in one ounce of water and maintained at blood heat for five consecutive hours lost 5 grains in weight. Thinking that if one could thus lessen the size of urinary calculi in a few hours it would be an easy matter to entirely remove them from the bladder, he advised the injection of solutions of lithium into the bladder for the cure of stone. In practice this was found to be unsuccessful, and it is interesting to note that the trial *case* in which Dr. Ure used the injections afterward came to operation and died.[4] Dr. Ure then showed that one must be very careful in the injection of lithium solutions into the bladder, for if any sodium phosphate be present the insoluble lithium phosphate is formed.

To show the effects that lithium carbonate had on the sodium urate in gouty deposits, Garrod made the following experiments:

A metacarpal bone having the phalangeal extremity completely infiltrated with gouty deposits was placed in water to which a few grains of lithium carbonate were added, and in the course of two or three days no deposit could be seen, and the cartilage seemed to have been restored to its normal state. Similar experiments made with sodium and

* Read before the Ann Arbor Medical Club, May 14, 1902.

potassium carbonates did not show any marked solution of the urates. It was reasoning from such experiments as these that lithium was introduced into medicine as a cure for gout. Of course, the fallacy of the treatment lies in the fact that lithium is a solvent for uric acid and urates only when in concentrated solution as well as in considering the diminished excretion of uric acid and urates as the chief pathological condition in gout.

To show that lithium in dilute solution was not a solvent for uric acid, Krumhoff[5] made the following experiments. To show the solubility of uric acid in distilled water at body temperature, he weighed out 0.5 g. of the pure acid and placed it in a flask containing 200 c.c. of distilled water. Four other flasks were similarly prepared. These were now placed on a water-bath so fixed that the flasks were completely covered in, and only a space was allowed for the thermometer to descend. The water-bath was at 39.5° C., and the flasks at 37.5° to 38.5° C. The heating was kept up for six hours. The flasks were then taken out, allowed to cool, the undissolved uric acid filtered off and thoroughly washed, dried, and weighed, when it was found that the 200 c.c. of water at body temperature had dissolved 0.0217 grain of uric acid. These experiments were confirmatory to similar ones done by Jahns,[6] who found 200 c.c. to dissolve 0.0214 grain in eight hours.

To show the solvent action of lithium chloride the following experiment was done: To 200 c.c. of water containing 0.5 grain of lithium chloride 0.5 grain of uric acid was added and placed on the water-bath under conditions similar to those in the last experiment, and heated for six hours. The undissolved uric acid was then filtered off, washed, dried, and weighed. Four other similar experiments were made, and the average of these showed that only 0.0118 grain of uric acid had been dissolved as against 0.0217 grain dissolved by distilled water under similar conditions. That lithium salts are solvents for urates and uric acid only when in concentrated solutions is not generally taken into consideration, and the majority of those who now administer lithium salts do so with the idea that they are uric acid solvents. The statements made as to the amounts of urates and uric acid eliminated after the use of the lithium salts vary greatly. Levy,[7] giving lithium bromide in gouty subjects, found the urates and uric acid diminished. Haig[8] and Oliver[9] found the uric acid diminished. Considering, however, that no constant diet was used, and also the faulty methods of estimation, these results can be considered of much value.

Dr. Garrod also claimed to have seen marked benefit derived from the external use of solutions of lithium salts applied to joints, even to the disappearance of small tophi. Hüfner,[10] to show that lithium salts were not absorbed through the skin, made a 1 per cent. solution of lithium chloride. This was warmed to 30° C., and one of his pupils

placed both feet in this for thirty or thirty-five minutes, and, although Hüfner was able, by the use of the spectroscope, to detect the presence of lithium in solution in the proportion of nine-millionths part of a milligramme lithium carbonate per c.c., he could not demonstrate lithium in the urine in this and similar experiments, even after the urine for twenty-four hours was taken and evaporated.

Hüfner could not find lithium in the urine after taking 25 milligrammes, even when the urine for twenty-four hours was concentrated to 30 c.c., but after taking 35 milligrammes, lithium could be plainly demonstrated in the urine two hours afterward.

The lithium salts are rapidly absorbed from the stomach. Dr. Bence Jones[11] gave an animal 3 grains of lithium chloride on an empty stomach and detected lithium in the aqueous humor of the eye and in the cartilage of the hip-joint fifteen minutes afterward. He gave 7 grains to a parturient woman eight hours before delivery, and found lithium in the umbilical cord. He also records giving 20 grains to a patient three and a half hours before an operation for cataract, and at operation traces of lithium could be detected in the lens. Four days later it could be detected in the secretions, and was not wholly eliminated till the seventh day. I have detected lithium in the saliva within eight minutes and in the urine and feces within ten minutes after injecting 1 grain subcutaneously in a cat.

The effect of lithium salts on animals was studied as early as 1868 by Rabuteau.[12] As a result of his experiments he concluded that lithium was a harmless metal, being less poisonous than potassium. He noted, however, that 20 grains of lithium sulphate given to a dog caused vomiting and evacuation of the bowels. He only observed the dog for a few hours and does not state the final results. In 1873 James Blake[13] experimented with lithium, and concluded that lithium, sodium, rubidium, tellurium, and cæsium are equal in their action, and that the amount of lithium sulphate necessary to kill rabbits was 1 grain per kilo.

In 1875 Hesse[14] experimented with lithium on frogs, rabbits, and doves. He found that lithium chloride injected into a vein caused diastolic stopping of the heart, while the nerves and muscles were yet excitable. He also found that in warm-blooded animals lithium salts decreased the excitability of the nerve centres, decreased the temperature, and sometimes caused diuresis. Cash and Brunton,[15] experimenting with the metals on frogs, found that lithium, rubidium, and cæsium have a tendency to affect either the upper part of the spinal cord or the higher motor centres connected with the forelimbs, the reflexes disappearing sooner from the arms than from the legs, and that stiffness was noticed in the arms. They also found the motor nerves paralyzed to a greater or less extent by lithium and potassium.

In 1884 Krumhoff[5] made a careful experimental investigation of the effects of lithium on animals, and reviewed the literature thoroughly. He found that when a lithium salt was injected into the blood it depressed the heart's action and caused a fall of blood pressure, and if the dose was large enough stopped the heart in diastole. The dose of lithium salts necessary to stop the heart he found to be much larger than the dose of potassium salts necessary to produce the same effect. He also found that vomiting and diarrhœa were caused by its subcutaneous use, and the prolonged ingestion of small doses killed the animal sooner or later by causing a fatal gastro-enteritis.

The lesions found at autopsy were hemorrhages into the stomach and bowels, reddening and swelling of the mucous membranes, and sometimes small hemorrhages into the heart muscle. The prolonged use of small doses of potassium salts caused no such effects.

To carefully study the effects of lithium salts on animals and determine where it was excreted, I made thirty odd experiments on cats and dogs, administering the drug subcutaneously and by the mouth. The salt used in my experiments was the chloride, because of its easy solubility and because the carbonate, which is usually used therapeutically, is in part, at least, changed to the chloride in the stomach. A pure salt was used and was examined quantitatively for lithium, as well as titrated for chlorides, so that the dosage might be accurate.

The method of quantitative estimation which I used was as follows: The urine, saliva, or feces to be examined was evaporated to dryness and burned. This was then extracted, with a large amount of water, rendered acid by hydrochloric acid, filtered, and the filtrate evaporated to about 50 c.c. To this milk of lime was added and thoroughly rubbed up until alkaline in reaction. This was then filtered and thoroughly washed with water until the washings failed to show lithium by the spectroscope. To this solution ammonium carbonate in solution was added as long as a precipitate formed, filtered, and the filtrate washed with water till the spectroscope failed to show any lithium in the washings. This filtrate was now acidulated with hydrochloric acid and evaporated in a platinum dish to dryness, and heated to drive off the ammonia. The residue was dissolved in water acidulated with hydrochloric acid and evaporated to dryness. This residue consisted of potassium, sodium, and lithium chlorides, and as the chloride of lithium is soluble in alcohol, while the chlorides of sodium and potassium are nearly insoluble, the dry salt was extracted with equal parts of absolute alcohol and ether. Comparatively small amounts were used, and the undissolved portion, after being washed with equal parts of alcohol and ether, was dissolved in water and examined by the spectroscope. If this showed the presence of lithium the process was repeated. In this way I was able to separate most of the sodium and potassium chlorides

from the lithium chlorides. The alcohol-ether solution was now evaporated to dryness, dissolved in a little water, and a 10 per cent. solution of sodium phosphate added, 1.1 c.c. for each 0.1 g. of lithium excreted. This was now evaporated to dryness, whereby the soluble lithium chloride was changed to the insoluble lithium phosphate. To this a small amount of water was added, heated slightly, and an equal amount of strong ammonia solution added, and let stand for twelve hours in the cold. As the lithium phosphate is practically insoluble in the strong ammonia solution, while the phosphates of sodium and potassium are freely soluble, the undissolved portion was lithium phosphate. This was now filtered through a Goosh filter, washed with a solution of strong ammonia, and this first wash-water again run through for lithium. The Goosh filter was now placed in an oven, thoroughly dried, and the weight of lithium carbonate determined, which was calculated back to the chloride.

By this method the lithium phosphate always shows a strong sodium flame, and the results are probably high. Yet, by becoming accustomed to the method, fairly accurate results can be obtained.

Only a few experiments will be quoted in detail.

Experiment 31, March 21, 1902. Healthy cat, weighing 1650 g., was given 1 g. lithium chloride, well diluted, hypodermically, at 10.40 A.M. At 10.45, movement of bowels, hard-formed. At 10.48, vomited; consisted of mucus and undigested food. An examination of this by the spectroscope showed the presence of lithium. At 11.05, marked salivation. At 11.10, vomited. At 11.30, movement of bowels. At 2.30 P.M. the cat had passed two or three diarrhœal stools. She sat humped up in the cage, and would not stir. By 5 P.M. she had had two more movements of the bowels and had vomited once.

22d. At 9 A.M., cat very weak, unsteady on feet. Drinks, but will not eat. Several diarrhœal stools during the night. He passed some urine, but not a great deal. At 5 P.M., cat in about the same condition, although weaker.

23d. Cat much weaker. Unable to walk without tottering. Hind-parts seem most useless. Will not eat or drink. No stool or vomiting. About normal amount of urine.

24th. Cat died during the night.

Autopsy Findings. March 24th, 11 A.M. Weight, 1405 g. All the organs were normal in appearance, except the stomach and intestines. The mucous membrane of stomach was reddened, and in two places showed hemorrhagic spots the size of a small pea. Mucous membrane of the small bowel not much inflamed, but covered with a thick, tenacious bile-stained mucus. The mucous membrane of the large bowel distinctly reddened and thickened, and contained two small ecchymoses. All the vomited matter, the stools, and the contents of the stomach and bowels were added together, and from them 0.086 g. lithium chloride was obtained. A microscopic examination was made of parts of the heart muscle, liver, kidneys, stomach, and intestines. The heart, liver, and kidneys showed no appreciable changes. Sections of the stomach

and bowel showed a marked congestion. The mucous membrane was covered with a thick coating of mucus, and in places contained small hemorrhages.

Experiment 5, November 11, 1901. A healthy cat, weighing 3700 g., was given 2 g. lithium chloride, well diluted, hypodermically, at 1.35 P.M. At 1.40, watery stool. At 2.00, passed urine. At 2.10, vomited. At 2.20, washed out stomach. At 2.40, thin, watery stool. At 3.10, washed out stomach. At 4.00, washed out stomach. At 5.00 cat was killed with chloroform.

Autopsy. Stomach contained mucus and water, which were added to vomitus and stomach washings. No marked change in the stomach walls. Bowels empty, and showed no marked change. Liver, kidneys, lungs, and heart apparently normal. The vomitus and stomach washings were kept separate from the bowel contents and stools, and the lithium in each estimated. The former contained 0.125 g. lithium chloride and the latter 0.034 g.

Experiment 10, November 25, 1901. A healthy cat, weighing 1320 g., was given 0.5 g. of lithium chloride, well diluted, hypodermically, at 1.20 P.M. At 1.30, vomited several times; 1.40, profuse watery stool. Up to 4.00 had vomited several times and had several watery stools.

26th. 1.00 P.M. Cat seems quite normal. Has not vomited nor had movement of the bowels during the night. Has passed considerable urine. When taken out of the cage seems stiff and perhaps somewhat unsteady on her feet. She drinks, but will not eat.

27th. 1.00 P.M. Cat more feeble than yesterday. When taken from the cage she is so stiff and weak that she can hardly walk. Hindparts seem most useless. No vomiting. No stools. Will not eat or drink.

28th. 1.00 P.M. Cat the same, but weaker.

29th. 1.00 P.M. Cat extremely weak. Unable to walk. Seems to be unable to raise her hindparts. No stools or vomiting.

30th. Cat died during the night.

Autopsy. Cat weighed 1080 g. The lungs, heart, liver, and kidneys were normal. Mucous membrane of the stomach reddened and covered with a thick, bile-stained mucus. Two small ecchymoses into the mucous membrane near the pylorus.

Small bowel somewhat congested and covered with a thick, tenacious mucus. Otherwise normal. Large bowel deeply congested. Several areas of hemorrhage into the mucous membrane, which is greatly thickened. The vomitus was worked separately from the stools, and from the former 0.021 g. lithium chloride, and from the latter 0.026 g. lithium chloride was obtained.

Microscopic examinations of the various organs showed no evident changes in the lungs, heart, liver, and kidneys, while the changes in the stomach and bowel corresponded to those given under Experiment No. 31.

Experiment 9, November 22d. A healthy cat, weighing 2650 g., was given 1 g. lithium chloride, well diluted, hypodermically. This experiment is of interest chiefly in that the cat did not vomit, but was salivated profusely. This salivation was undoubtedly due to nausea, and was observed in many experiments before vomiting came on. All the saliva was carefully collected in a clean dish, and, as it showed lithium by the spectroscope, the amount was estimated quantitatively, and

0.021 g. lithium chloride was obtained from it. The cat died in three days with all the signs of gastro-enteritis, and from the stools, stomach, and bowel contents 0.110 g. of lithium chloride was obtained.

These experiments have been given in detail, because they show the essential symptoms and cause of death from lithium salt in whatever form or manner it be administered. From these experiments it will be seen that shortly after the administration of the lithium salt the animal is taken with nausea, vomiting, and diarrhœa, and dies sooner or later with all the characteristic signs and symptoms of gastro-enteritis, the progressive emaciation and weakness being wholly the result of the gastro-enteritis. The stiffness and inability to use the hindparts is also due to the weakness caused by the gastro-enteritis, and is seen in poisoning from the heavy metals, colchicum, and other drugs that cause a fatal gastro-enteritis. There is practically a total absence of nervous symptoms, although in a few cases slight tremors were noticed. This is of importance, as tremors have been noted in a few cases of poisoning in man.

From these experiments it will be seen that lithium is partially excreted in the saliva and into the stomach and bowels, though the quantity that can be reclaimed from these secretions is usually not great.

To show the effects of the prolonged administration of small doses hypodermically, the following two experiments may be given:

Experiment 12, December 3d. A healthy cat, weighing 3170 g., received each day for eighteen days 0.0567 g. lithium chloride, well diluted, hypodermically. She had diarrhœa on the second day, which was severe by the fourth day, when the stools were blood-streaked. The urine and stools were kept separate. The diarrhœa was severe, and she occasionally vomited. On the tenth day she had lost 500 g., or about one-sixth of her original weight. Her coat had lost its gloss, and her health and strength distinctly lessened. By the eighteenth day she was very weak, weighed 2650 g., had a severe diarrhœa, and, as it was quite evident that she would soon die, she was killed with chloroform, as I wished to examine the tissues in a perfectly fresh condition.

Autopsy Findings. The lungs, kidneys, liver, spleen, and heart were apparently normal.

The stomach did not show any marked changes. The upper part of the small intestines was quite normal, but the lower one-fifth, together with the large bowel, was deeply congested. The mucous membrane was thickened and showed numerous small and large hemorrhagic areas. There were two small superficial ulcers in the large bowel, which was more severely affected than the small bowel, and, I may add, that this is unfortunately the case when small doses are administered, whether given subcutaneously or by the mouth. The stools and urine for the first ten days were examined for lithium. During this time she had been given 0.567 g. lithium chloride. From the bowels 0.039 g., and from the urine 0.228 g. of lithium were obtained.

Experiment 14. In order to accurately collect the urine a healthy female dog, weighing 8.2 kilos., was operated upon, the perineum being

cut so that she could be easily catheterized. After the wound had thoroughly healed, and beginning February 7th, she was given 0.62475 g. of lithium chloride, hypodermically, daily. She was not allowed to pass any urine, being catheterized frequently enough to prevent this. The urine and stools were kept separate. At the end of ten days her weight was 8.1 kilos., and she was lively, ate and drank well, and apparently had not suffered from the injections. From the ten days' urine 0.383 g. lithium chloride was obtained, and from the feces 0.074 g. of lithium chloride. She had received in this time 0.62475 g. of lithium chloride.

The same dose was continued eight days longer, and at this time she began to show symptoms, such as loss of appetite and a slight diarrhœa. On the eighteenth day she weighed 7.9 kilos. Her coat was roughened, and she was evidently in poorer condition than at the beginning of the experiment.

The injections were then stopped until February 4th, when they were again taken up, increasing the dose to 0.2479 g. From the second day on she vomited occasionally, usually consisting mostly of mucus. There was a slight diarrhœa. Her appetite was very poor. The injections were continued for six days. At the end of this time her weight was 7.1 kilos. From the six days' urine 0.589 g. and from the feces 0.014 g. lithium chloride was obtained. During the six days she had been given in all 1.5 g.

The injections were now increased to 0.62475 g. daily. This was continued for five days. During this time she vomited several times a day and had a severe diarrhœa, the stools being often streaked with blood. She ate scarcely anything, and at the end of the experiment weighed 7 kilos. She was very weak and emaciated. Coat rough and lustreless.

From the five days' urine 1.49 g. and from the feces 0.128 g. of lithium chloride was obtained. During the five days she had received 3.1 g. The injections were now stopped, but the vomiting and diarrhœa continued unabated. The appetite was completely lost, and she became weaker daily. On February 24th she was so weak that she was hardly able to stand, and as it was evident that she would soon die, she was killed with chloroform. At this time she weighed 6.8 kilos. At the beginning of the experiment she had weighed 8.2 kilos., a loss of 1.4 kilos in weight.

Autopsy. Heart showed a few small hemorrhages under the endocardium, otherwise normal. Lungs, liver, and kidneys normal. The walls of the stomach were greatly thickened and reddened, and contained several small hemorrhages. The mucous membrane of the whole bowel was thickened and reddened, though this change was most marked in the large bowel. The lower part of the large bowel contained a few small ulcers and numerous ecchymoses.

Microscopic examination of the heart showed only a few small hemorrhages under the endocardium. Lungs, liver, and kidney showed no marked changes. The examination of the stomach and bowel showed congestion and thickening of the mucous membrane, with a superficial layer of mucus and detritus, and one or two small superficial ulcers.

One hundred grammes of the muscle from the ham were burned and the ashes dissolved in 30 c.c. of distilled water. This gave a distinct

spectroscope of lithium, even when diluted to 90 c.c. One hundred grammes of normal dog's muscle when burned and the ashes dissolved in 30 c.c. gave no lithium spectroscope, even when concentrated to 5 c.c.

The ashes from 100 g. of blood taken from this dog showed lithium, even when diluted to 130 c.c. That from normal dog's blood gave only a faint spectroscope when dissolved in 5 c.c. water. It is evident from this that lithium is slowly excreted and is stored up in the body. The liver did not show as much lithium as an equal weight of muscle.

When lithium salts are given by the mouth they produce essentially the same symptoms and changes as when given hypodermically, though, of course, larger doses are required. Cats, after receiving 0.5 to 2 g. by the stomach, vomit two or three times, but otherwise are very little affected, though frequently some diarrhœa is noticed. On the contrary, when small doses are administered daily by the mouth, cats and dogs show first diarrhœa, with some blood in the stools, vomiting, loss of appetite, and weight, and finally die from the gastro-enteritis, as the following experiment well shows:

A healthy cat, weighing 2000 g., received daily for the first six days 0.062475 g. by the stomach. No symptoms at this time, though she had lost 100 g. in weight. The dose was now increased to 0.125 g. daily, which was continued for five days; during this time she developed a moderately severe diarrhœa, and at the end of six days weighed 1800 g. The dose was now increased to 0.188 g. daily, and was continued for fifteen days. During the most of this time she had a severe diarrhœa, the stools often containing blood, and during the latter part of the period she was nauseated, and vomiting constantly, and finally died of gastro-enteritis and exhaustion, weighing 1500 g. At autopsy there was found a marked inflammation of the whole gastro-intestinal tract. This was most severe in the large bowel, which contained many large and small ulcers and ecchymoses. There was also some enlargement of the abdominal lymph glands and two or three small abscesses in the liver, undoubtedly secondary infections from the bowel.

In some experiments the animals that were given lithium in small doses lost over one-third of their weight, and finally died of exhaustion and gastro-enteritis. Sixty milligrammes of lithium chloride per kilo. daily always killed dogs and cats sooner or later from gastro-enteritis. Though frequently, especially in dogs, this was much delayed by the animals vomiting the lithium solution soon after taking it.

The cause of this gastro-enteritis is undoubtedly connected with the excretion of the metal through the bowel wall. This action on the bowel is not peculiar to lithium, but is caused by many other substances, among which may be mentioned mercury, arsenic, colchicum, emetine, and aloin. These substances are excreted by the bowel, and also in the urine, and induce irritation or inflammation at the point

excreted. This may be because they collect in larger quantities in the excretory organs, or because they are here freed from some harmless combination in which they have circulated in the tissues. At times the bowels are most affected, and *at other* times the kidneys suffer most. Lithium salts are slowly excreted by the kidneys and do not seem to cause any appreciable amount of renal irritation. On the contrary, the excretion through the bowel causes marked irritation and inflammation. The percentage of lithium salts obtained from the feces in my experiments was always greater in those cases accompanied by marked vomiting and diarrhœa.

There are very few cases mentioned in the literature of poisoning from the use of lithium, and it is not generally considered as inducing any deleterious symptoms. Wood, in his text-book of *Therapeutics*, says he has seen a twenty-grain dose of lithium carbonate produce a severe general prostration in a feeble adult female; and Hare, in his *Practical Therapeutics*, says: "It is worthy of note that in some cases citrated lithium will disorder the stomach and produce vomiting." In a note to the French edition of Garrod on *Gout*, the statement is made that small doses are readily borne, but doses of thirty to fifty grains of the carbonate give rise, after a few days, to cardialgia and dyspepsia. Rabuteau states that 15 to 30 g. per diem often causes dyspepsia, and even vomiting. Climent[17] records similar results in his own person, and Althaus[18] states that lithiated waters, if taken in large amounts, give rise to sickness and diarrhœa. Kolipinski[19] reports two cases of marked tremor following the use of lithia tablets. This was also accompanied by marked general prostration and weakness. The condition disappeared in three or four days. Considering the marked effect of lithium salts on animals, it is surprising that symptoms on the part of the gastro-intestinal tract have not been noticed more frequently. It is not improbable that such symptoms have frequently been noticed, but have not been reported, or have been considered as due to other causes. It might be stated here, however, that lithium is frequently given as the natural lithia waters, which, as shown by the analyses of Harrington,[20] Waller,[21] and others contain only very small amounts of lithium, many containing none at all.

Lithium salts are frequently credited with the possession of diuretic action. To determine whether they possessed any marked diuretic action I made several experiments on rabbits, as follows: Large rabbits were anæsthetized with urethane and paraldehyde. A canula was introduced into the jugular vein and one into the bladder, so as to be able to inject the fluids into the blood and to collect the urine.

After determining the normal flow of urine, warmed solutions of equal strength of lithium chloride and sodium chloride were injected into the vein and the urine collected and measured. In order to have

the solutions contain equal numbers of molecules, they were so prepared that their freezing points were the same. Solutions containing about 3 g. and 6 g. of lithium chloride and sodium chloride, respectively, in 100 c.c. of distilled water were used, and from 30 to 50 c.c. were injected at the rate of 15 c.c. in five minutes. The results of these experiments did not show that solutions of lithium chloride caused any greater diuresis than solutions of sodium chloride.

The salt of lithium used in medicine is the carbonate. It is much less soluble than the chloride, and experiments on animals show that it produced the same effects as the chloride. The bromide of lithium has been used in the treatment of gout, epilepsy, and other nervous diseases. Dr. Weir Mitchell,[21] after using lithium bromide in several cases, concluded that it was as efficient as sodium or potassium bromide, and that its influence over insomnia was greater.

Fontan[22] found lithium bromide to possess the same sedative action as potassium bromide, but he thought it less liable to cause untoward symptoms. Dr. Mitchell, however, saw skin rashes following the use of lithium bromide. Lévy[24] found lithium bromide to possess marked sedative action, and to be less depressing to the heart than potassium bromide. He did not, however, find it to be of any special value in gout.

Since the atomic weight of lithium is so small, there is, of course, more of the bromide ion in lithium than in an equal weight of potassium bromide, and the action of the bromide ion completely overshadows the action of the lithium ion. Lithium bromide does not possess any advantages over the commonly used potassium bromide.

Conclusions. 1. Lithium is excreted in the saliva, into the stomach and bowel, and in the urine. The greater amount is excreted in the urine, though more appears in the stomach and bowel when nausea, vomiting, and diarrhœa have been profuse. It can usually be demonstrated in the secretions within ten minutes after a hypodermic injection, though its excretion proceeds slowly, for I have found it in the secretions twenty-three days after the injections were stopped.

2. Lithium salts given to animals, hypodermically or by the stomach, cause, sooner or later, fatal gastro-enteritis. This gastro-enteritis is, undoubtedly, connected with the excretion of the metal through the bowel wall.

3. Lithium salts do not possess any diuretic action that cannot be accounted for by their salt action. They render the urine alkaline, and thus act like the other alkalies.

4. Lithium carbonate, in fifteen to twenty-grain doses, and lithia tablets have been known to cause gastro-intestinal symptoms in man.

5. Dilute solutions of lithium salts are not solvents for uric acid or urates.

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URETERITIS IN THE FEMALE.

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A CONVENIENT classification of ureteritis is the following:

Simple ureteritis.

Ureteritis with obstruction.

Tubercular ureteritis.

SIMPLE URETERITIS. This form may be either acute or chronic. In the acute cases parturition seems to have a decided influence as an etiological factor. Hallé[1] and Morris[2] think that the pressure of the child's head, by causing trauma, offers a favorable soil for the development of the disease. Primiparæ are especially affected. The disease is ushered in with chills and fever, and a condition of general sepsis is the result. There is pelvic pain and vesical irritation, and pressure vaginally over the affected ureter is very sensitive. In a few days after the onset of the disease pus may be seen in the urine in large amounts. If the kidney is seriously affected the prognosis is grave, and death may ensue.

[1] Urétérite et Pyélite, Paris, 1887, p. 148.

[2] Surgical Diseases of the Kidneys and Ureters, London, 1901, vol. ii. p. 398.

The diagnosis of acute ureteritis of this nature is difficult unless one recognizes the possibility of the disease. Pyelonephritis is more easily recognized from focal symptoms. It is doubtful if simple acute ureteritis ever exists alone, and if it does, it can be diagnosed as such. Usually it is part of a pyelitis or of a cystitis, and the symptoms of these affections so overshadow those of the ureteritis that the latter escape detection.

Diphtheritic ureteritis has been found at autopsy. In the Boston City Hospital records there are 2 such cases occurring in 3424 autopsies. In the first case the bladder and both ureters were covered with the typical black membrane, and in the other the renal pelves and upper part of both ureters were affected.

Chronic Ureteritis. A ureteritis may be the sequel of either a vesical or a renal inflammation, and as vesical inflammations are more common than the renal, we usually find a chronic cystitis associated with the ureteritis. Infection from a ureteral fistula is easily understood. Infection from the diseased bladder would be more common if the valve at the ureteral opening did not act as a determined barrier to the entrance of germs, and when we consider the large number of cases of cystitis we must allow, from the relatively rare occurrence of ureteritis, that the valve does in reality act as a barrier in this way. I have seen in a case of tubercular cystitis infection resisted for five years by the remaining kidney and ureter after nephrectomy for the opposite tuberculous kidney. But that this valve does not always act in this way has been abundantly proved by the experiments of Young[1] and of Lewin and Goldschmidt.[2] They all found that injection of methylene blue under high pressure and rapidly would not result in reflux of the dye into the ureters of animals, but that if injected slowly reflux would sometimes occur. Coutade and Guyon[3] also experimented in the same direction, and found that if the bladder were injected in this way—*i. e.*, largely and slowly—reflux into the ureter occurred in two-thirds of the cases in rabbits and in one-fifth of the cases in dogs. Hallé[4] lays particular stress on the method of invasion of the inflammation into the ureter by means of direct extension of the inflammation along the mucous membrane, and he brings in support of this view the fact that lesions around the ureteral orifice and bladder are older in appearance than those in the ureter. He believes that reflux of septic urine into the canals must be of relatively rare occurrence. In the rare cases of urethral stricture in the female, the mechanism of infection is the same as that in the male. There is retention of urine in the bladder and later stagnation of urine in the ureters. This

[1] A. H. Young. Johns Hopkins Hospital Bulletin, 1898, No. 86, p. 105.
[2] Virch. Archiv, 1893, vol. cxxxiv. p. 33.
[3] Leçons Cliniques sur les Maladies des Voies Urinaires.
[4] Op. cit., p. 132.

leads to dilatation, first of the ureters and later of the ureteral orifices; infection is then easy by direct invasion into the ureters of the germs in the bladder when the bladder contracts in its expulsive efforts.

The gonococcus is the germ most to be dreaded as a cause of ureteritis, on account of its well-known disposition to result in stricture. Ureteritis may occasionally originate from calculous pyelitis, and the infection may reach the bladder, where it may cause characteristic changes, to be described later. The infection from pus-tubes, inflamed lymph glands, and pelvic cellulitis has been known to cause ureteritis, the infection in these instances travelling through the lymphatics.

The pathology of the disease is that of mucous membranes elsewhere in the body. There is reddening of the tissues and desquamation of the epithelium. Occasionally the inflammation extends through the ureter to the tissues around it. The symptoms will vary with the extent of the urinary tract involved. If the kidney has been the starting point of the disease, or if the kidney has been affected secondarily by an ascending infection, we may expect some renal pain or at least some discomfort in the lumbar region on the affected side. This sign is by no means constant, however, and it may be absent. As the bladder is generally if not always affected, the symptoms are mainly referred to it; so we find frequency of micturition the chief symptom. The desire to urinate never leaves the patient, and it constitutes the principal source of suffering. The calls to urinate vary with the degree of severity of the disease and with the stage. There are temporary remissions, but these can hardly be called remissions, as the suffering is constant, even during these. Generally the patient has to empty the bladder at least once an hour by day and several times by night. Occasionally urination is required every fifteen minutes by day and ten or twelve times by night. The act is usually painless, but sometimes pain is experienced deep in the bladder, on one side, in the vicinity of the affected ureter. The pain in these cases is of an aching character, and it may last as long as half an hour after the act of urination. Tenesmus may or may not be present, and incontinence is very rare. Perhaps the most distressing source of suffering is that caused by the excessive degree of neurasthenia which is the inevitable result of the incessant suffering and the loss of sleep. The patient is very apt to lose flesh, is irritable, peevish, and has no object in living. The digestion is disturbed and constipation is common. Headaches are experienced and also the typical pressure feeling on the top of the head, as well as the various neuralgias so often accompanying severe degrees of neurasthenia.

The most important sign on physical examination is the greatly increased tenderness of the affected ureter when pressed upon vaginally as compared with the opposite ureter. When the ureter is thus pressed upon there is a coincident extreme desire to urinate, which is with diffi-

culty controlled by the patient. If the ureter has been diseased a long time it is possible that there may be some enlargement which may be discovered vaginally. It is difficult to see how a moderately thickened ureter could be felt through the abdominal walls unless these were very thin or relaxed. But pressure along the course of the ureter is often elicited, especially at the pelvic brim, and this is an important diagnostic sign.

On cystoscopic examination the trigone and vesical neck will be found congested to a more or less degree. There may be patchy cystitis on the posterior wall, but usually if the affection has lasted some time the bladder as a whole will present a relatively normal appearance. The most important sign which I have observed in these cases of simple ureteritis is swelling of the ureteral eminence on the affected side. As compared with its fellow on the opposite side it is much larger, especially if viewed with the patient in the knee-chest position. Besides this, it is invariably red and at times streaky, the streaks proceeding from the ureteral opening. The entrance to the ureter on the summit of the eminence is swollen and puffy, and at times the mucous membrane inside the canal may be everted so that it presents as a small red spot. Ulcerations are rare even if the affection has lasted for years.

There is one sign presented by the examination of the urine which I have found of the greatest diagnostic importance, and this is an excess of desquamated epithelium, which may or may not be associated with the presence of pus on the affected side. This epithelium may be free or in sheets, and it is medium-sized or small, round, or spindle shaped, or even squamous. If the inflammation is confined to the ureter, and the renal pelvis is not affected, pus is always in very small amounts, and, as has been mentioned, may be entirely absent or imperceptible. This same peculiarity is also seen even in the tubercular forms of ureteritis if the ureter alone is involved—*i. e.*, there may be a considerable excess of epithelium, and very little pus. Occasionally blood corpuscles are seen, and if the kidney has been invaded a few granular and hyaline casts may be found.

The utmost care must be taken in collecting the urine from the ureters so that there shall be no admixture with vesical elements, and also that trauma during instrumentation shall be avoided. For this purpose the only serviceable cystoscope is that of Kelly, which has the oblique end. With this instrument the urine drops into the end of the tube directly from the ureter, and may be collected in a bottle at the outer end of the tube.

Reynolds[1] has called attention to the fact that the amount of urea on the affected side as compared with the opposite side is diminished,

[1] Gynecological Transactions, 1896, No. 21, p. 282.

and he brings eight cases in support of this view. My experience has been similar, and I am inclined to think that the ureteral inflammation must exert an inhibitory effect on the excretion of the urinary solids. I have observed the same peculiarity in a case of renal calculus associated with ureteral calculus, although the kidney when removed, with the exception of the stones in it, was apparently healthy, there having been no suppuration. The separated urines before operation showed a marked difference as regards the urea excretion in favor of the sound side.

The amount of urine will often be scanty, and Mann has seen it as low as 180 c.cm. in the twenty-four hours. It is usually acid in reaction, and has a low specific gravity. It must not be supposed that the amount of urine is always low, for cases will be met with in which the amount is normal or nearly normal.

The diagnosis of simple ureteritis is sometimes a very difficult matter. Most frequently it is not recognized at all, and the case is treated for years perhaps as a chronic cystitis or as a reflex bladder trouble of nervous origin. It is well then in the presence of such a case to proceed at once to a cystoscopic examination. This gives the most important aid in making a diagnosis. The characteristic lesions of the ureteral eminence of the affected side combined with the swollen appearance of the eminence itself, and also the study of the urinary sediment, will direct attention to the seat of the trouble and will be sufficient to establish the diagnosis. A vaginally tender ureter is an important sign.

There is one affection of the ureter with which ureteritis may be confounded, and that is ureteral stricture; but as stricture is a sequel of the disease, and as ureteritis always accompanies stricture, this is perhaps not the best way to put it. If stricture is suspected on account of the long duration of the case, passing graduated bougies will at once clear up the diagnosis. Tuberculosis of the ureter as a primary affection probably never occurs alone, and need not enter into the differential diagnosis. It is always a part of a renal or a vesical tuberculosis, or both, and the symptoms and signs of either are usually sufficiently marked to allow of a diagnosis being made. Salpingitis and ovaritis may be mistaken for ureteritis, and the failure to relieve symptoms by removal of the ovaries and tubes may be due to the fact that the coexisting ureteritis was not recognized. This error ought not to occur. Other inflammatory pelvic disorders, such as appendicitis, have been mistaken for ureteritis; a careful study of the case will clear up the diagnosis.

The prognosis of the disease is very poor if it has lasted a long time; but if recognized early, and it has been properly treated, the prognosis is encouraging. In the very chronic cases treatment has been very unsatisfactory, and alleviation of symptoms has been all that has been

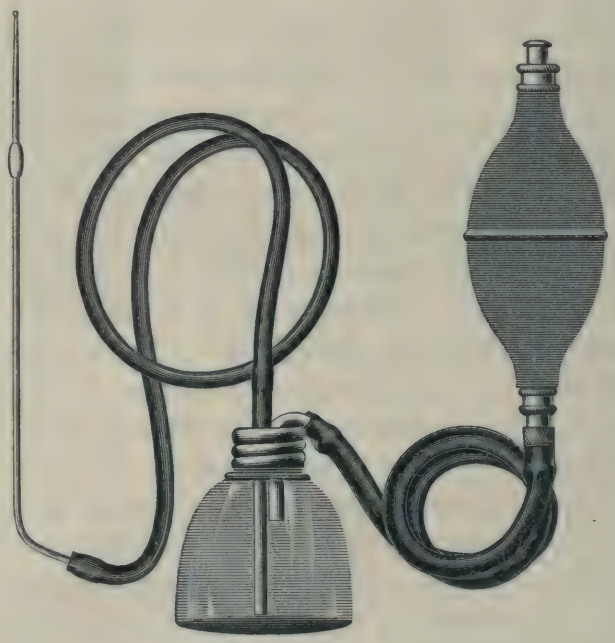
accomplished. All methods of treatment have been tried, but most of them have been found to be of little value. The difficulty lies in the fact that the disease is situated in such a small tube in the centre of the body that it cannot be reached by direct means. The treatment has been largely palliative, therefore, and has been confined to the administration of drugs combined with general hygienic measures. Much may be accomplished in this way, and these measures should always be insisted upon. As a preliminary to treatment a diseased tube or ovary, if it lies over the course of the ureter, should be removed. The same applies to other diseased pelvic conditions. The diet should be carefully regulated with reference to the kind of food given. It should be bland and nutritious. Too much nitrogenous food should be avoided, and also those foods which tend to make the urine irritating, such as asparagus and rhubarb. A simple diet of farinaceous food should be given, such as eggs, soups, broths, fresh green vegetables, the white meat of poultry and game, occasionally beef, mutton, or lamb, plenty of milk, and, above all, a large amount of water. If the stomach is irritable it may be difficult to select the proper diet. Mann has seen excellent results follow a restricted milk diet. Attention to the bowels is of importance, as a loaded colon pressing on the ureter is productive of pain. The function of the skin should receive attention, and hot baths and rubbings are recommended. The patient should take the fresh air every day, if she is able to be out and if exercise is not fatiguing; if it is, sitting out in the air is the next best thing.

Regularity of living is essential. The patient should retire early, and she should likewise take a good deal of rest in the recumbent position in the day-time. Overexertion invariably aggravates the condition. The drugs usually of benefit in vesical inflammations may be tried. If the urine is acid, decided benefit will be derived from giving acetate of potassium in large doses. Sandalwood oil sometimes relieves symptoms, but it is irritating to the stomach. Urotropin is sometimes of value, but it appears to do most good in cases in which there is a large amount of pus in the urine. Bicarbonate of soda in large doses may be tried, particularly if there is acidity of the stomach; it is sometimes of great value. Alcohol should be avoided. For general tonics, iron, arsenic, and strychnine may be given. Morphine should never under any circumstances be given, on account of the great danger there is of forming the habit. Patients tolerate the disease many years without recourse to morphine, and it is quite unjustifiable to use it. A good remedy for sleeplessness is trional; one or two 10-grain doses at night will generally give some sleep, and it may be freely used. No habit is formed, and it may be withdrawn at will.

Topical applications to the bladder have done much good in these cases. A solution of nitrate of silver in a 5 or 10 per cent. strength

applied to the trigone and to the ureteral eminence once or twice a week gives considerable relief. A vesical injection of a 5 per cent. solution of protargol or a 50 per cent. solution of ichthyol have proved satisfactory. About 2 drachms of either may be injected, and the injection should be retained at least half an hour.

The rational method of treating the ureteritis itself would seem to be by means of topical applications to the ureteral canal. The instrument shown in the figure is one which I devised for injecting the ureter through a cystoscope in the bladder. It consists of a long, straight silver tube with a blunt-pointed extremity and a bulbous expansion a short distance from its end. A rubber tube connects the instrument



with the reservoir bottle containing the fluid to be injected, which fluid is forced by air pressure into the silver tube by means of a rubber hand-bulb. By working the hand-bulb the silver tube is filled with the fluid, and in this condition, the air having been thus expelled, it is introduced into the ureteral orifice. The instrument enters the canal, and is pushed along it until the bulbous expansion reaches the ureteral orifice. A little extra pressure is now exerted so that the bulbous expansion may come in close contact with the orifice in order to prevent regurgitation of the fluid injected. Quite considerable pressure with the hand-bulb is now exerted, and the ureter and renal pelvis are injected. That the fluid is really injected is evidenced by seeing it come out of the ureteral orifice in a strong stream when the instrument is with-

drawn. The patient experiences some pain in the ureter, but it is tolerable. Occasionally she complains of some backache in the region of the kidney injected. I have proved by an experiment on the cadaver that the whole renal pelvis can be injected in this way. A solution of methylene blue was used and the instrument used in the way described. When the kidney and ureter were subsequently opened they were found to be deeply stained with the dye; all parts of the renal pelvis were of an intensely blue color. The only solutions which I have yet tried, for the instrument is new, have been boracic acid, 2 per cent., and nitrate of silver, 1 per cent. They were well tolerated. The treatment was done in my office, and the patient returned home unaccompanied. As to the results of this treatment it is too early to say, for I have done it only a few times. The patients upon whom it was tried always experienced relief after the applications, especially during the night following the treatment, and they had to get up to urinate less often than ever before.

If all means have failed to relieve the symptoms and these are urgent, the only remedy left is the making of a vesicovaginal fistula; but even this will not in all cases relieve the symptoms wholly, for the irritation, being in the ureter, is still present, and the nagging desire to urinate although relieved in a measure, may not entirely disappear. If there is well-marked cystitis the fistula should be made; some relief will be sure to follow.

Mrs. F. P., first seen in December, 1899, was forty-three years old, had been married twenty years and had had seven children. Three years before she had an attack of severe colic in the lower part of the abdomen, the attack having come on immediately after the birth of the youngest child. Since then there has been urinary trouble. When first seen she was urinating every few moments, the pain being always felt on the left side of the bladder, in the vicinity of the left ureteral orifice and ureter. Besides this there was also pain in the urethra. There were some dyspeptic symptoms attended with flatulency and constipation. The general health was poor, and she was very nervous and irritable at times, and her sleep was much disturbed.

An examination showed a lacerated cervix and perineum, cystocele, and rectocele. Abdominally both kidneys were negative, but upon pressure over the course of the left ureter it was sensitive, especially at the lower end, and vaginally the finger discovered a very sensitive and somewhat enlarged ureter, which when pressed upon excited an intense desire to urinate. A cystoscopic examination showed a red urethra, vesical neck, and trigone. The left ureteral eminence was larger than the right one, and it presented a swollen and puffy appearance; it was quite red, and its orifice was somewhat pouting. The right ureteral urine collected with the oblique-end cystoscope was normal. The left ureteral urine was acid in reaction, and its sediment, evident to the eye and imparting a turbidity to the urine, showed a great excess of medium and small round cells, likewise numerous caudate and spindle cells, as

well as a few casts and some blood corpuscles; there was no pus. There was one peculiarity which was particularly noticed while collecting the ureteral urine which I have not before observed in any case, and this was that while the right ureteral urine came away in strong jets at frequent intervals, the left ureteral urine was scantier in amount and came away in jets occurring at longer intervals than on the right side. By estimation only half the amount of urine flowed from the left ureter during the time that twice the amount flowed from the right, and the jets on the left side occurred at twice as long intervals as those on the right, and they were feebler in force. This observation is in line with the diminished urea excretion in these cases.

The patient was put upon a regulated diet, and was told to drink a large amount of water and to take the fresh air every day. Besides this, local applications of nitrate of silver in the strength of 5 and 10 per cent. were made to the trigone and ureteral eminence every few days for a long time. After having been under treatment a few months she underwent an operation for the cure of the lacerations. The operation was successful, and since it was performed the bladder symptoms have been decidedly less troublesome. The internal medication consisted in taking urotropin, acetate of potassium, and bicarbonate of soda. Later, injections of a few drachms of a 5 per cent. solution of protargol into the bladder, which were retained half an hour, seemed to do a great deal of good. Most relief has been obtained by injecting the ureter with a 1 per cent. solution of silver nitrate at intervals of a few days. On the whole the patient is decidedly better, but she is by no means well, and still suffers a good deal from the pain on the left side of the bladder; and urination, while it has been reduced by the treatment to four or five times a day and once or twice at night, is still quite painful. The case illustrates very well how meagre our therapeutics are in this class of urinary disease. The patient has been very faithful in following every detail of treatment during the past three years, and while she is by no means well, she considers that she would have been much worse had she not been under treatment.

Ureteritis with Obstruction. The obstruction may be partial or complete, and, according as this is the case, symptoms and changes will vary. The changes differ also according as infection has taken place or not. If it has not taken place, and the obstruction is complete, we may get simple hydronephrosis. If this happens on one side only it may be the only permanent change, and the final result, if the obstruction is not removed, is complete atrophy of the kidney. Inflammatory changes in such a case are likely to supervene if the obstruction has been caused by an inflammatory mass pressing upon the ureter, such as a purulent salpingitis. In such an event pyonephrosis becomes engrafted upon a hydronephrosis. Infection in such a case may also proceed from the kidney itself, the result of germs excreted by it. Albarran[1] has shown that secondary infection is common and that the germ most frequently found is the bacterium pyogenes.

[1] Etude sur le Rein des Urinaires, Paris, 1889, p. 105.

The causes of strictured ureter are given by Morris as follows: (1) Valve of mucous membrane near renal pelvis; (2) valve caused by obliquity of ureter to renal pelvis; (3) fibrous stricture (gonorrhœal); (4) ureter compressed by branch of renal artery; (5) calculus in the ureter; (6) fibrous band at the brim of the pelvis; (7) twist of the ureter on its long axis; (8) compression of the ureter by enlarged lymphatic glands; (9) conversion of the ureter into an impervious cord. Of all these causes, those which are usually associated with inflammatory changes are fibrous stricture and calculus. These two only will therefore be discussed.

Obstruction may be partial or complete. By partial obstruction is meant that the urine always has sufficient passage to flow through the narrow canal, and that the stricture is never so tight as to even temporarily occlude the urinary canal at the diseased point. The symptoms of this class of cases will proceed, therefore, from the accompanying ureteritis rather than from the stricture itself. By complete obstruction is meant that the canal is completely occluded or that it is subject to intermittent closures. The result is practically the same—ultimate disorganization of the kidney above.

Partial Obstruction. Fibrous Stricture. The chief cause of fibrous stricture is gonorrhœal infection. The stricture may, however, result from ureteritis from other infections, and also from trauma inflicted by the passage of a renal calculus. Occasionally external inflammation around the ureter will result in stricture. It is very probable that many cases of strictured ureter in the past have been diagnosed as neuroses, cystitis, hyperæmia of the vesical neck and trigone, reflex irritable bladder, etc., because the chief symptom of the disease is frequency of micturition. This obscurity has been due to the difficulty of arriving at the correct diagnosis, for it is made solely by instrumentation. The duration of the disease, untreated, is practically chronic. In one of my cases the duration was twenty-five years, the patient having suffered all that time. The symptoms of the gonorrhœal cystitis glide imperceptibly into those of the ureteritis; and as they are nearly identical, the patient is treated for the cystitis alone, and no attention is paid to the ureter, the chief seat of the chronic disease.

The symptoms of the disease are those of simple ureteritis, and they need not, therefore, be repeated in detail. We have the renal pain and distress if the kidney has been invaded; it is not usually marked, and it is not elicited, as a rule, from the patient unless special attention is directed to it. The urinary symptoms are in part due to the cystitis usually present in these cases, in part to the inflammation of the ureter itself, for we find when the cystitis is cured or almost cured that frequent micturition, attended or not with pain, still persists. The chief distress comes from the constant desire to urinate, which

never leaves the patient. This desire to urinate is peculiar. The patient is never satisfied, and she always feels that if she could only empty the bladder satisfactorily she would be relieved. The phrase "nagging desire to urinate" was used by one of my patients to describe the sensation felt. Tenesmus and incontinence are the same as in simple ureteritis. Neurasthenic symptoms, as one would expect from the long duration of the disease, are of a marked character. The patients are wretched and miserable. The tender ureter is found vaginally, and the cystoscopic appearances are the same as in simple ureteritis, and need not be repeated. The streaky appearance of the eminence and the swollen eminence itself are noticed. The separated urines have the same characteristics as in simple ureteritis without stricture, and I would especially insist on the presence or excess of desquamated epithelium on the affected side, with or without pus and blood corpuscles. The total amount of urine may be diminished, and a quantitative analysis will show a diminished excretion of solids. It is acid, of low specific gravity, and may contain a slight amount of albumin.

The diagnosis is at once made with the ureteral bougies. On passing these in turn into the ureter one will be found which will be arrested at a certain point, the seat of the obstruction. If more than one stricture exists in the same ureter the diagnosis of the high ones is impossible unless the lowest one is of greater calibre than the higher. There are normal narrowings in the ureter, and the mistake should not be made of confounding these with pathological strictures. These normal narrowings are found, according to Van Hook,[1] at the following points: the first is at a point between four and seven centimetres from the renal pelvis, the second is where the ureter curves over the pelvic brim (in three out of five), and the third is at the junction of the vesical and ureteral portions.

The prognosis of strictured ureter has been sufficiently intimated. It is a long-standing affection, and it is very difficult to cure. The chief source of danger is on the part of the nervous system, which is constantly irritated; and even if the patient is cured, months may elapse before the mental equilibrium is re-established.

The treatment of the affection should have for its end the complete restoration of the lumen of the canal. Dilatation of the stricture has been proposed, and it has this to recommend it, that it does not involve a cutting operation. The number of reported cures by this method of treatment is as yet so few that we cannot form any idea of its position as a therapeutic measure. We do know, however, that it will give relief from symptoms. The chief objection to the method is that it is extremely painful at times. Urinary fever and chills occasionally follow

[1] Surgery of the Ureters, Journal of the American Medical Association, December 1, 1893.

ureteral dilatation, and Morris[1] relates a case in which the vesical orifice of the ureter was torn in an attempt to dilate a high stricture. The orifice subsequently became completely closed. If it is desired to attempt dilatation it is best to use either Kelly's graduated renal catheters or the French ureteral bougies. These should not be passed more than once or twice a week. If gradual dilatation fails, or if the patient will not submit to it, one of the operations recommended for the cure of the condition may have to be performed. The best one is that which exposes the ureter through an extraperitoneal incision after preliminary introduction of a ureteral catheter. The stricture may then be cut upon the catheter and the two angles of the incision united together by means of fine sutures. The sewing should not be done until the rest of the canal has been explored for high strictures. If the stricture is of great length, and it happens to be situated near the bladder, it is advisable to transplant the ureter, which may be cut off just above the stricture, into the summit of the bladder. Any stricture below the pelvic brim may be treated in this way. If there is a long stricture high up, and transplantation is not practicable, the only other resource is nephrectomy or the establishment of an artificial loin fistula. The condition of the opposite kidney and the general state of the patient should be considered in choosing between the two operations. Simple cystotomy in these cases has been tried, but the relief given thereby is very slight, because the spasm and pain, dependent as they are, upon the ureteral lesion, continue just the same after the cystotomy. This has been the experience of others as well as my own.[2] The only indication for cystotomy is coincident violent inflammation of the bladder.

Miss M. F., first seen in June, 1896, was forty-five years old. The vesical symptoms came on immediately after an attack of gonorrhœa, twenty-five years previously, and she has never been free from vesical suffering since then. The first symptoms of acute cystitis glided imperceptibly into those of chronic cystitis and ureteritis. There was increased frequency of micturition, attended with pain, and there was great distress from the constant desire to empty the bladder, which was never absent. There was a good deal of tenesmus, but never incontinence. Some pain was experienced in the region of the right kidney and also along the course of the right ureter at the level of the pelvic brim. There was some backache. Sleep was much disturbed, and the nervous system was a complete wreck. She was very irritable, had no object in living, and frequently threatened to commit suicide. On examination there was no tenderness over either kidney, but later this sign was present over the right one. Along the course of the right ureter there was no tenderness except at a point just above Poupart's ligament; here there was a good deal of sensitiveness on pressure.

[1] Surgical Diseases of the Kidney and Ureter, London, 1901, p. 440.

[2] See case reported by H. A. Kelly in Johns Hopkins Hospital Bulletin, 1891, p. 240.

Vaginally the right ureter was somewhat enlarged, and pressure on it was very painful and excited an intense desire to urinate. On cystoscopic examination the urethra, vesical neck, and trigone were much congested, and the right ureteral eminence, which was redder than the rest of the bladder, also had a streaky appearance; it was larger than the left eminence. The right ureteral urine showed a sediment of a great excess of epithelium, some casts, and an appreciable amount of pus. The left ureteral urine was not remarkable. The stricture of the ureter was not discovered for a long time, because it was not thought best to pass a catheter into the ureter through the infected bladder. In a similar case with a history of gonorrhœa it would be justifiable to do so.

The treatment of the case was that recommended for cystitis and ureteritis; but after a few months of treatment, no great improvement having been accomplished, a vesicovaginal fistula was made. This gave a tolerable existence for as long a time as it was allowed to remain open, which was five years. During this time she was relieved from the necessity of emptying the bladder, but she still had the nagging desire to urinate, which persisted in spite of the free drainage afforded by the fistula. When the fistula was closed, at the urgent solicitation of the patient, the old symptoms returned. In October, 1901, the stricture was discovered in the right ureter, at a point eight centimetres from the ureteral eminence. The stricture admitted a 1-millimetre probe. Dilatation was at once begun, and it soon admitted a 3-millimetre probe. Relief followed, and the nagging desire to urinate became much less in a short time; but it did not entirely disappear, and it has not up to the present time, owing to the persistence of the ureteritis. Lately injections of the renal pelvis have been instituted, and were given with the apparatus described in this paper. These have been well supported, and have given further relief. The patient is now in the best condition that she has ever been in, the ureteral injections always relieve her, and she usually has a good night's rest after the treatment. There is still an excess of epithelium on the right side, but the pus has entirely disappeared.

Calculous Obstruction. It is not intended to enter into a complete discussion of calculous disease of the kidney and ureter, for that would extend the limits of this paper far beyond that intended. Reference will be made in a brief way to the symptoms and diagnosis of the affection and to the consequent ureteritis which it entails.

The narration of a typical case is perhaps the best way to describe the disease.

Mrs. F. C., aged twenty-five years, was first seen in July, 1898. She had been operated upon by Dr. W. H. Baker, of Boston, for salpingitis, in February, 1898, and panhysterectomy was performed Seven years previously there had been an attack of true renal colic caused by a renal calculus, which was subsequently seen when passed *per urethram;* since then there had been urinary trouble. Five years after the onset of the trouble there was an attack of hæmaturia, the blood persisting for two days. The usual symptoms of cystitis and ureteritis were present. There was frequent and painful micturition, attended with tenesmus. In addi-

tion to this there was constant pain in the left hypochondriac and lumbar regions, which pain radiated into the bladder and vulva. Decubitus was always painful on the right side, and riding in the cars was painful as well as movements of a sudden nature. On physical examination there was no tenderness on pressure over either kidney, but there was a good deal of tenderness over the left ureter when it was pressed upon at the pelvic brim, and pressure on the ureter vaginally was very painful, and in this part of its course it was enlarged. On cystoscopic examination the urethra, vesical neck, and trigone were found to be scarlet red, and the whole bladder wall was streaked with red streaks one or two centimetres long and one or two millimetres wide; there were likewise small patches of the same nature scattered throughout the bladder. The left ureteral eminence was larger than normal, and on its surface, as well as on the surface of the trigone about it, there were very many small, yellowish dots, one millimetre in diameter, circular in outline, and of punctate appearance, as though punched out with a punch. The eminence bled easily on being touched. Scattered throughout the bladder were many small, whitish elevations (enlarged lymph follicles), resembling sago grains. The right ureter was easily catheterized, but not the left, owing to a tight stricture of the ureter situated eight centimetres from the bladder. The right ureteral urine showed a urea percentage of 1.13 per cent., and was of pale color, of acid reaction, and the sediment, considerable in amount, showed some pus free and in clumps, a few caudate and medium-sized cells, and a few granular and hyaline casts. The left ureteral urine, collected with the Harris segregator, showed a urea percentage of 0.4 per cent.; it was of pale color, of acid reaction, and the sediment was the same as in the right ureteral urine, except that the amount of pus was much larger. No tubercle bacilli were found in any of the specimens of urine, and guinea-pig tests were negative as regards tuberculosis. The treatment of the case was at first palliative, but as the pain in the kidney became more severe an exploratory incision was made in February, 1900. A large stone was found in the pelvis of the left kidney, and, as there were several other stones in the renal parenchyma, the kidney was removed. The stones were of the calcic oxalate variety. A probe passed into the ureter was arrested at the pelvic brim, and an X-ray picture taken later showed the obstruction to be a stone. Subsequent events justified leaving the stone in the ureter, for it has never given any trouble. No special treatment was given for the cystitis after the operation, and when the patient was last seen, in January, 1902, the bladder was perfectly normal. As she complains of pain in the right kidney occasionally, it is feared that there may be a stone in it as well.

What is most remarkable in the case is that while the bladder was the seat of violent inflammation, the renal pelvis was of normal appearance, in spite of the presence of calculi in it. The suggestion is at once offered that the stone in its descent was arrested by the pus-tube, and that ureteritis followed by continuity; the inflammation then spread downward into the bladder, and not upward at all. I would especially call attention to the vesical appearances in this case. The small punctate ulcers were quite characteristic, and I have never seen them in any other bladder that I have examined. Their grouping around

the affected ureter suggests a causative relation between them and the calculus, but one cannot draw conclusions from a single case.

The diagnosis of ureteral calculus may be made by a careful consideration of the details of the case. Occasionally[1] stones are lodged in the ureter, and they give no symptoms at all, and they may be passed several months later without discomfort. Usually, however, there is a history of previous pain in the kidney and along the course of the ureter, and there may have been attacks of renal colic with hæmaturia. If the patient has seen calculi in the urine, additional evidence is thereby furnished. The vesical symptoms are suggestive and point to cystitis, although there are cases of concomitant vesical irritability in which no true inflammation exists in the bladder, the irritability being due in such cases to reflex causes. The examination of the urine will throw considerable light on the nature of the disease, particularly the examination of the separated urines, and it is far better in securing the separated specimens to make use of Kelly's oblique-end cystoscope in order that adventitious blood corpuscles may be absolutely avoided; this, in view of the fact that it frequently happens that the blood in the urine in cases of calculi of the upper urinary passages is sometimes very scanty in amount, while its diagnostic importance is very great. The absence of pus does not exclude calculus, for it will not be found if infection has not taken place. The lessened urea excretion on the affected side is characteristic and shows the effect of inhibitory influences. The same peculiarity may be noticed in cases of ureteritis, as has already been mentined. Cystoscopic appearances are suggestive. The punctate ulcers may prove to be of diagnostic importance, but as I have seen but one case it may merely go on record; confirmatory evidence is needed. Occasionally the ureteral stone may be felt through the vagina, and in such a case the diagnosis is at once plain. Finally, the X-ray may be employed in determining the diagnosis, and the wax-tipped bougie may be passed. Abbe[2] records 27 cases of stone detected in the ureter by means of the X-ray. Leonard[3] in a series of 206 cases had 65 positive results. In these cases ureteral calculus was more frequently found than renal. Leonard believes that some skill is required in reading the negatives, for the shadow of the stone is not always distinct.

The differential diagnosis lies between cystitis, ureteritis alone, appendicitis, and other pelvic inflammatory affections. Tuffier[4] called attention to the fact that a concretion lying in the appendix will sometimes give a radiograph picture which closely simulates stone, and he advises passing a wire into the ureter in order that it may be photo-

[1] Fenger. American Text-book of Genito-urinary Diseases and Syphilis, 1898, p. 496.
[2] Annals of Surgery, August, 1899, p. 198.
[3] Philadelphia Medical Journal, February 11, 1902, p. 222.
[4] La Semaine Médicale, August 9, 1899.

graphed with the concretion; the different locations of the wire and the concretion will readily eliminate stone in the ureter. It would seem that symptoms on the part of the bladder, including cystoscopic examination and urinary analysis, should direct attention to the true cause of the disturbance. This applies also to other pelvic inflammations, such as prolapsed and adherent ovary, etc., but the possibility of both affections being present should be borne in mind.

The prognosis depends on the degree of obstruction and whether infection of the upper urinary passages has taken place or not. If it has not taken place the patient may have the disease for many years, and suffer meanwhile from the kidney, ureteral, and bladder symptoms, which become tolerable. If infection takes place, general symptoms of a more severe nature occur, and surgical interference may be imperative. If the kidney has become diseased in consequence of the obstruction, and the obstruction is finally removed, the renal function may be resumed, and repair takes place in the renal tissue, but obstruction must not have lasted more than a few months.

The treatment of partial calculous obstruction will depend on the length of time the calculus has been lodged in the ureter. Occasionally it may remain in the ureter some days, and is then passed; it is well, therefore, not to be in too great haste before relieving the obstruction. When, however, the obstruction has existed an appreciable length of time, operation should be decided upon. In all cases the operation should be extraperitoneal, for it is possible to reach the ureter in any part of its course by appropriate incisions. The ureter having been exposed, the stone is removed, the incision in the ureter closed by fine sutures, and the external wound closed, with drainage. In a list of nine cases cited by Fenger[1] seven were of the extraperitoneal variety and two of the abdominal; six of the former recovererd and one died; and of the latter, one recovered and one died. In seventeen cases recorded by Tuffier and mentioned by Fenger, only three died, and in these three patients the opposite kidney was diseased. If the kidney is damaged, or if there are stones in the renal parenchyma, the question of nephrectomy comes up. If the kidney is removed it may not be necessary to remove stones in the ureter, because they may become encapsulated and may give no further trouble; but one must be sure that there is no secondary periureteritis around the stone before it is abandoned in this way. Sometimes the stone has almost reached the bladder, and may be seen with the cystoscope projecting at the ureteral orifice; an alligator forceps will often succeed in removing it.

Complete Obstruction. Fibrous Stricture. As has already been stated, fibrous stricture may exist in the ureter for many years

[1] Loc. cit., p. 499.

without ever becoming so narrow as to completely occlude the lumen of the canal; but there are cases in which the narrowing progresses gradually until the canal is finally completely occluded either intermittently or permanently. The subsequent changes being the same in either instance, we may therefore consider them both in one class. The inevitable result is pyelonephritis in the kidney above.

Acute obstruction of the complete variety, caused by a virulent germ, gives rise at once to acute pyelitis and pyelonephritis, the symptoms of which are of such a marked character that there is usually no difficulty in making the correct diagnosis.

The chronic cases, on account of the obscure symptoms, are of greater interest. One would naturally suppose that a chronic pyelonephritis in which the cause has been a stricture of the ureter would present symptoms referable to the kidney of so pronounced a type that there would be no difficulty in diagnosing the renal affection at once. Such is not the case. A kidney will sometimes go on to complete destruction without ever giving more pronounced symptoms than an occasional backache or uneasiness in the lumbar region. In these cases the vesical disturbances are the chief cause of suffering. One would also suppose that the general health would suffer to such a degree in these cases as to constitute a symptom of prominence; but I have seen a case in which the patient, a robust woman, maintained her general health and strength, as well as her mental equilibrium, to a marked degree, and she had suffered for many years from her stricture and from the ureteritis and pyelonephritis accompanying it. I would not be understood as saying that with a pyelonephritis the general health is never seriously undermined, for this is not the case, and the majority of patients will present general symptoms of a marked character; but I insist that even in these cases the kidney may not attract attention to itself by such decided focal symptoms as to direct attention to itself as the chief cause of disturbance. Watson[1] has recorded a very remarkable case of double-strictured ureters, which is of such interest that I wish to refer to it briefly. The patient was a young man, aged twenty-one years, who had contracted gonorrhœa one year previously. The inflammation had apparently subsided, and there was no symptom to indicate that the kidneys were damaged; but after exposure to cold a year after the apparent disappearance of all symptoms the patient was suddenly seized with chills, fever, and general prostration. The urine was diminished in amount and contained some pus and albumin; then for the first time a tumor was noticed in the left hypochondriac region, which was incised; the contents were purulent urine. Death ensued five days after the onset of the acute symptoms. At the autopsy strictures were

[1] Journal of Cutaneous and Genito-Urinary Diseases, No. 9, p. 407.

found in both ureters. The right kidney was the seat of extensive pyelonephritis, and the left one was transformed into a pyonephrotic sac. There had been no symptom on the part of the kidneys to attract attention to them. Watson in the same article refers to five other cases of a similar nature, only one of which was in a female; of the whole six cases, in three there were no focal symptoms on the part of the kidneys until within three days of death. In all six cases strictured ureters, with subsequent pyelonephritis, were present.

Secondary changes in the ureter are dilatation above the point of stricture and great thickening of the fibrous coat of the tube. The dilatation may be so extreme as to readily admit the forefinger into the lumen. Rupture is rare, although it may occur. Below the point of stricture the ureter is inflamed, and the inflammation may extend into the bladder. In the kidney the inflammatory changes are those usually seen in pyelonephritis. Dilatation of the renal pelvis occurs in the first instance if the obstruction has been gradual, and finally the inflammation attacks the cortical and medullary substance, producing in them abscesses of small and large size. The kidney is finally reduced to a mere capsule, inside of which there are septa which mark the site of previous abscesses. The entire renal tissue has been destroyed. If the patient survives, and nothing has been done, the final stage may be inspissation and drying up of the pus, and the process comes to an end. Such a result is hastened by the establishment of a fistula in the groin, either as the result of an operation or from natural causes; but the patient may succumb to the effects of the disease before this occurs, and death is usually due to some acute inflammatory exacerbation. Before concluding the subject of secondary changes it may be observed that the same changes may occur in consequence of stricture of the urethra in the female, and that in these rare instances both ureters are affected. A remarkable example of this sort is recorded by L. B. Tuckerman,[1] in the case of a girl, only five years old. She had always suffered from enuresis, and on one occasion only had had pain in both loins. There had been hæmaturia also. At the autopsy both ureters were found dilated and diseased as well as both renal pelves. The entire urinary tract was in a state of purulent inflammation. There was stricture of the urethra, of what nature is not stated.

Symptoms. The symptoms referable to the bladder are those principally complained of. They are the usual symptoms of cystitis, and need not again be enumerated in detail. Pain attending the act of micturition may be present or absent. When present it may be extreme, causing the greatest agony. Pain along the course of the ureter may sometimes be experienced, but as a rule it is not of diagnostic

[1] New York Medical Record, February 15, 1902, p. 280.

importance. Of the renal symptoms, pain is the principal one when it does occur. The pain is referred to the loin or the hypochondriac region, and may radiate into the lower part of the abdomen, even into the labium of the side corresponding to the diseased kidney. A dull aching in the loin is often complained of, and a feeling of distress especially on exertion. Sometimes the pain is not at all localized, and may be felt as a general backache in the lumbar region, being equally severe on either side. Fever is by no means a constant symptom, and Albarran[1] has shown that in more than one-half the cases of renal suppuration caused by obstruction, fever is entirely absent. There may, however, be acute attacks of pain in the kidney, and these may be accompanied by prostration, with nausea and vomiting, sweating and fever. In such cases we may suspect a temporary complete occlusion of the stricture by a shred of necrotic tissue. During such an attack there is elevation of temperature, with chills and fever and general prostration, which last until the lumen of the canal has become patent again. The urine during an attack is clear, and when the attack is over there is a large discharge of purulent urine, which brings relief with it. As for general symptoms, they include headache, anæmia, muscular weakness, disinclination to work, fatigue on slight exertion, and gastro-intestinal disturbances. The latter are very commonly found accompanying renal affections. The duration of the foregoing symptoms may be many years if the condition is not properly recognized and treated.

On physical examination we may derive important information. Bimanual examination of the bladder sometimes elicits pain; and if we examine the suspected ureter at the same time we may find that it is enlarged and boggy if the stricture is low down and the obstruction is complete, so that a condition of pyoureter exists. If the ureter is very much enlarged it may be felt abdominally, but the cases are rare in which this can be done. Over the kidney region, in the hypochondrium, just below the ribs, pressure with the hand will generally evoke resistance of the abdominal muscles. This is a valuable sign indicative of inflammatory renal disease. Bimanual examination of the kidney may detect enlargement if this is present. Fluctuation is rarely detected unless there is a large amount of fluid in the kidney.

The changes viewed through the cystoscope may be those seen in a chronic cystitis with constant reinfection. There is great injection, affecting the whole surface of the bladder, especially in the neighborhood of the vesical neck and trigone. Small superficial ulcerations are scattered about here and there, especially in the vicinity of the ureteral orifice corresponding to the diseased side. The ureteral orifice is

[1] Étude sur le Rein des Urinaires. Paris, 1889, p. 106.

sometimes quite deeply eroded if ulcerative changes are at all marked, and there may be considerable difficulty in locating the orifice, owing to the destruction of the landmarks. In such a case the opening may be sometimes found by seeing a gush of pus and urine well up from the bladder, in the vicinity of the spot where the eminence should be. The separated urines give evidence of value. On the affected side pyuria is marked. The amount of pus is always excessive, and collects at the bottom of the glass in quite a deep layer. This large amount of pus is quite diagnostic of pyelitic affections. Hallé[1] relates a case in which toward the end of life 300 grammes of pus were voided in twenty-four hours. The pus may have a fetid odor. Albumin is present in large amounts. The specific gravity is very low, and the reaction is usually acid unless the infection has been produced by one of the germs giving rise to alkalinity, such as the proteus vulgaris.[2] The sediment contains the usual elements—casts, various forms of epithelia, and blood corpuscles.

Some difficulty will sometimes be experienced in passing the stricture with even a small-sized ureteral catheter; usually, however, with patience and continued effort this difficulty is overcome. When the stricture has been passed a gush of accumulated urine and pus rushes out of the catheter and at once establishes the diagnosis.

Four courses are open for consideration in the treatment of fibrous stricture with pyelonephritis and violent cystitis: The first is nephrectomy; the second is gradual dilatation of the stricture with bougies, combined with repeated washings of the renal pelvis with antiseptic solutions carried up to the kidney by means of a long renal catheter; the third is the performance of a cystotomy, with the idea of relieving the distressing symptoms on the part of the bladder and of allowing the kidney to go on to complete destruction, in the hope that it will atrophy and give rise to no further disturbance; the fourth is making an artificial fistula above the strictured portion of the ureter.

If it is tolerably certain that the kidney has ceased to be actively functionating, as determined by the examination of the separated urines, the methylene blue test, and by cryoscopy, and it is fairly certain that it is not worth saving, the idea of nephrectomy may be entertained. Nephrectomy may sometimes become imperative, as, for instance, when a general infection of the body threatens. Perinephritic abscess sometimes supervenes in these cases of pyonephrosis; and if the symptoms incident to such a complication are marked, as they are quite certain to be, the safest treatment is preliminary incision and evacuation of the pus, and secondary nephrectomy later, when the patient has recuperated from the acute septic condition.

[1] Loc. cit., p. 113.

[2] T. R. Brown. Johns Hopkins Hospital Reports, 1901, vol. x., Nos. 1 and 2, p. 28.

The treatment of pyonephrosis associated with stricture by means of dilatation of the stricture, combined with repeated washings of the renal pelvis with antiseptic solutions, has much to recommend it, and it is especially to be considered in those cases of pyonephrosis which have not yet been of sufficiently long duration to have destroyed a very large portion of the renal parenchyma. The method consists in passing the renal catheter up to the renal pelvis through the stricture, which is at the same time dilated; antiseptic solutions are then allowed to flow through the catheter, and local treatment is thus given every few days. Kelly[1] records a case treated in this way. The patient was a female, aged thirty-one years, with a spiral stricture of the ureter. The stricture was dilated with ease up to 6 millimetres, and the kidney and ureter treated with washings of bichloride of mercury solution in the strength of 1 : 150,000 to 1 : 16,000, and of nitrate of silver solution in the strength of 1 per cent. The infection was cured and the pus disappeared; but in spite of the dilatation of the stricture there still existed a condition of hydroureter, and the accumulated urine above the stricture was 100 cubic centimetres. Kelly thought the hydroureter to be due to loss of elasticity of the ureteral walls. Pawlik[2] had a similar case of stricture, with pyoureter, which he cured after thirty treatments of the same nature as that employed by Kelly. Morris[3] reports another of Kelly's cases in which a stricture and pyoureter were treated in this way without success. The patient had six treatments at intervals of twelve days, but as each treatment was followed by exacerbation of pain and distress, it had to be abandoned; a ureterovaginal fistula was finally made for the relief of the pyonephrosis. It would appear from the report of these cases that the method is sometimes successful in relieving pain and distress, that it sometimes cures the patient, and that it is sometimes not tolerated at all.

It will sometimes happen that the patient will not entertain the thought of nephrectomy. In such a case it is essential to do something to relieve the distressing symptoms on the part of the bladder; but if the kidney is the source of considerable disturbance from the accumulation of purulent urine within it, simple cystotomy will not give much relief except in so far as it relieves the vesical symptoms. With a "silent" kidney, however, cystotomy will at once put the patient in a condition of comparative comfort, and she enjoys life once more. It is possible at the end of many months that the kidney process may come to an end, and the final stage of inspissation and atrophy takes place. It is conceivable under such circumstances that

[1] Operative Gynecology, vol. i. p. 438.

[2] Albarran and Lluria. Comptes Rendus de la Société de Biologie, 1891, vol. iii., No. 24, p. 543, and No. 26, p. 587.

[3] Surgical Diseases of the Kidney and Ureter, vol. ii. p. 439.

the patient might get entirely rid of her infection and recover, in which case the fistula might be closed.

A fistula above the stricture may sometimes have to be made if for any reason nephrectomy or other methods of treatment are impracticable. The indications are distressing focal symptoms on the part of the kidney. The fistula may be made into the vagina, provided the stricture is low enough, or it may be made into the loin if the stricture is a high one. Subsequent nephrectomy should be entertained if this operation is practicable, depending on the decision of the patient and her general condition.

Case I.—Mrs. C. F. B., aged thirty-five years, was first seen in September, 1898. She was a strong woman, of rather nervous temperament, but under good control. Symptoms had been of two-years' duration. Frequent micturition attended with pain were the first symptoms noticed. The desire to empty the bladder was constant, and urination was necessary every hour, day and night. The general health was excellent. On examination some sensitiveness was discovered over the course of the left ureter at the pelvic brim, and, vaginally, pressure over the same ureter was sensitive. On cystoscopic examination the urethra and whole bladder were generally injected, especially the left hemisphere, and particularly about the left ureteral orifice. The left ureteral eminence was covered and apparently obliterated by cicatricial tissue; its orifice was not seen, and the ureter was not catheterized at this examination. Around the left eminence were many small, superficial ulcerated areas, about one centimetre in diameter, which bled easily on being touched with a probe. At a subsequent examination the left ureter was entered, and a tight stricture discovered about six centimetres from the ureteral orifice. Immediately on passing the stricture there flowed from the catheter eighteen cubic centimetres of purulent urine, thus proving a condition of dilated ureter with retention. The right ureteral urine was not remarkable, and showed a urea percentage of 1.77 per cent. The left ureteral urine showed a urea percentage of 0.63 per cent. It was of a pale, turbid color, containing a trace of albumin; and the sediment, considerable in amount, consisted of pus chiefly, some medium-sized epithelium, a few round cells, and granular detritus; no tubercle bacilli were found. Guinea-pig tests were negative. As the patient refused any serious operation, an artificial vesico-vaginal fistula was made. Immediate relief followed, and she has been comfortable ever since. In this case there was undoubtedly a "silent" kidney which never gave any trouble. At present the patient is perfectly comfortable, and she steadfastly refuses operation of any kind. She has had her fistula nearly five years. Lately an X-ray photograph was taken, with a negative result as regards stone.

Case II.—Miss T., aged twenty-two years, was seen in January, 1897. Six years previously she had a fall from a hammock, and from that time her symptoms began. When first seen she was in poor general condition. She had lost a good deal of flesh, was very anæmic, and was very nervous and irritable. She had never had any pain in either lumbar region, and there had never been any symptoms on the part of the kidneys to attract attention to them. The usual symptoms

of cystitis were present in a marked degree, and constituted the principal source of suffering. On examination there was some resistance of the muscles over the right kidney, and vaginally the right ureter was larger than normal, and could be felt as a hard cord. The bladder showed the usual appearances of violent cystitis, including ulceration of the right ureteral orifice, which was entirely destroyed.

On catheterizing the right ureter a tight stricture was discovered a short distance from the bladder. The left ureteral urine was normal, but the right ureteral urine contained a large amount of pus, casts of the hyaline and granular variety, and different sized cells. The urea percentage was 0.63 per cent., while on the left it was 2.4 per cent. Guinea-pigs were inoculated, but the result was negative. In February, 1897, a lumbar incision was made and the kidney removed. It was entirely destroyed, with the exception of the capsule and a small amount of tissue underneath it. The ureter was much enlarged and thickened, and admitted the little finger with ease. The operation was entirely successful, and the symptoms rapidly disappeared shortly after it was performed. She was last heard from in June, 1899. She was then well and about to be married. There were no vesical symptoms.

Calculus in the Ureter. Complete obstruction due to calculus in the ureter has been, in the majority of cases, preceded by symptoms and signs pointing to calculus of the kidney. The effect of aseptic permanent closure of the ureter by this means is atrophy of the kidney within a few months, the organ becoming reduced to mere fibrous tissue. In the autopsy records of the Boston City Hospital is the report of a case in which a calculus was lodged in one of the two ureters leading from the same kidney. The portion of the kidney drained by this ureter was atrophied, while the other portion, which was the lower, was perfectly normal. Ralfe and Godlee[1] have recorded a remarkable case in which a calculus was present in either ureter simultaneously. Anuria followed, and an operation upon the right ureter discovered the stone impacted two inches below the pelvis of the kidney. The left ureter was then explored, but the stone was not found; it was passed later. If infection has been present in the pelvis of the kidney before the stone has descended into the ureter, or if it has taken place subsequently, pyelonephritis follows in the kidney. Pyonephrosis is the final ending, the kidney being reduced to a thick-walled cyst containing much or little pus. In some instances of ureteral calculus the periureteral tissue is inflamed, and abscess may occur, resulting in fistula, which may open into the loin. In the autopsy records of the Boston City Hospital is the report of a case which presents unusual features. The patient during life suffered from obscure abdominal symptoms referred to the region of the left kidney. Death resulted from general peritonitis, and at the autopsy the left kidney was found

[1] Clinical Society's Transactions, London, 1889, p. 155.

lying beneath a ruptured abscess cavity which had no connection with the kidney or its capsule. In the ureter were found two stones, one lying impacted 13 centimetres below the renal pelvis, and another a short distance below this; the ureter was not completely obstructed. Behind the ureter, and on a plane with the first stone, was a small abscess cavity, $3 \times 2\frac{1}{2}$ centimetres in dimension, in which there was a third stone; this cavity was in direct communication with the large abscess cavity directly in front of the kidney. What probably happened was gradual necrosis and solution of the ureteral wall, occasioned by the pressure of the first stone, which was the oldest one; then secondary abscess in the periureteral tissue; and, later, extension of the abscess to the region in front of the kidney.

The ureter itself may become thinned by pressure, or it may be greatly thickened and dilated. Below the calculus the ureter may become converted into an impervious cord. Changes in the bladder are those due to cystitis.

The symptoms of the affection are frequently obscure as regards location of the calculus. If high up calculus in the ureter cannot be diagnosed from calculus in the kidney, as the symptoms are identical in each. Sudden impaction is evidenced by severe renal colic and possibly hæmaturia. After the first attack of renal colic the pain gradually subsides, and then come on the symptoms of pyonephrosis. The course now varies according as the infection is virulent. If it is virulent, focal symptoms point to the affected kidney; or, on the other hand, with a mild affection the patient may relapse into a condition of toleration. The stone remains embedded in the ureter, and gradual disorganization of the kidney takes place. Some discomfort and uneasiness may be experienced on the affected side, with occasional pain in the lumbar region. Sometimes a tumor below the ribs may be felt by the patient. The cystoscope may show changes in the vicinity of the orifice of the affected side, especially if there has been preceding cystitis.

The urine in complete obstruction will not flow on the affected side, and this constitutes an important diagnostic sign. Periodical discharges of pus point to intermittent complete closure.

The diagnosis is made by a careful survey of the previous history of the case. Previous attacks of hæmaturia are of great diagnostic value, as are also attacks of colic. The X-ray should always be used to determine the seat of the stone; it will not always be successful in locating it. If an exploratory incision is made into the kidney the diagnosis of ureteral obstruction may be made by passing a sound into the ureter from above, but the same result is arrived at by ureteral catheterization through the vesical route. If the latter is done the nature of the obstruction cannot, however, be accurately deter-

mined. Vaginal touch will sometimes locate a stone, which may be felt as a hard mass under the examining finger.

The treatment of complete obstruction is surgical. As to the kind of operation selected, this will depend on the condition of the kidney and the length of time that impaction has existed. It is not proposed to discuss the various methods in detail.

Tubercular Ureteritis. The frequency with which tuberculosis affects the ureter may be seen by the following figures: In 3424 autopsies performed at the Boston City Hospital and at the Massachusetts General Hospital during the past ten years tuberculosis of the kidney occurred 64 times, of which cases 24 were of the caseous variety and 40 of the miliary. In the 24 caseous cases the ureter was diseased as well as the kidney; in the remaining cases it was not affected. In 194 cases of nephrectomies which I have collected from various sources, tuberculosis of the ureter was mentioned 27 times as a complication of the renal disease. Probably we may add to this number, allowing for cases not mentioned.

In this form of ureteritis the ureter may be greatly increased in size. Usually the canal remains patent in spite of its tortuosity and in spite of the numerous shreds which descend from the kidney. Sometimes it does become occluded in this way, and when it does dilatation of the canal ensues as well as more rapid destruction of the renal tissue above. This dilatation may sometimes reach an enormous size, and the cavity thus formed may hold many ounces of pus.

The symptoms referable to ureteritis are so masked and overshadowed by those produced by the renal and vesical tuberculosis that they attract little attention. The main symptom, and the one which may excite suspicion, at least, that the ureter has begun to be involved, is colic. This is produced by a shred of tissue which is caught in the ureter as it descends.

On physical examination, if the disease has lasted any length of time, thickening of the ureter will always be found on vaginal examination. This thickening is quite characteristic of the disease. It is readily detected by the finger, and it is felt as a solid cord running toward the pelvic brim. It is very tender to the touch, and pressure on it excites an urgent desire to urinate. Abdominally an enlarged ureter may be felt through the abdominal walls if the patient is thin, but not otherwise. The appearances seen through the cystoscope are characteristic, and are sufficiently marked to allow of a diagnosis being made in the majority of cases. The typical tuberculous ulcers, with their raised edges and excavated appearance, are very apt to be situated near the orifice of either ureter, generally to the inner side, and miliary tubercles may be seen in the vicinity. In a very advanced stage of the disease, when the mucous membrane of the whole bladder

has been sloughed off, there may be cicatrices and corrugations. In such a case the diseased eminence may have disappeared as the result of the ulcerative changes, and there may be some difficulty in finding the ureteral orifice. The urine gives changes such as would be expected in pyelonephritis. There is abundant pyuria, and the amount of albumin is large; casts, renal elements, shreds, and lastly the tubercle bacillus are found. If, however, the tuberculous disease has not gone beyond the limits of the ureter, and has not invaded the kidney, the amount of pus may be very slight; this is a sure indication that the kidney has not been seriously involved, for with a large secreting cavity in the kidney the amount of pyuria on the affected side is always large. The diagnosis is easy. If a hard, thickened ureter is felt vaginally, tuberculosis may be strongly suspected. Additional evidence is furnished by the history of the case, the cystoscopic appearances, and focal symptoms on the part of the kidney. Finding the bacilli confirms the diagnosis.

It will be interesting to give the results of operations which have been performed upon the ureter for tuberculosis. To the 194 cases of tuberculosis which I have examined may be added Bangs'[1] list of nephrectomies, to the number of 135, and Facklam's[2] list, to the number of 86, making a total of 415 nephrectomies. Among these cases total nephro-ureterectomy was done 16 times, with but 1 death. The results were most excellent. Of the 16 cases 3 have survived two years or more and 1 of them four and a half years, and all the rest were doing well at the time of the report except one, which was improved only. The case which has survived four and a half years is one which occurred in my own practice. The patient was a girl of twenty, and nephro-ureterectomy was done in two sittings, and the tuberculous bladder cauterized throughout on two occasions under ether. She is perfectly well to-day, and does not exhibit a sign or symptom of tuberculosis. Of the partial resections of the ureter with nephrectomy there were 10, with no mortality; 1 of these died later; 3 were improved; in 3 the duration was not given, but they were doing well; and in the other 3 the progress was satisfactory. Of the cases among the 415 nephrectomies in which the ureter was known to be diseased, but was abandoned, there were 36. Analyzed, these cases were as follows:

[1] Annals of Surgery, 1898, No. 27, p. 20.

[2] Die Wegen Nierenphthisie Vorgenommenen Nephrotomien, etc. Archiv. für klinische Chirurgie, 1893, vol. xlv. p. 715.

Total number			36
Operative deaths		11	
Operative recoveries		25	
Percentage of operative deaths			30 per ct.
Operative deaths		11	
Pulmonary phthisis	3		
Tuberculosis of opposite kidney	2		
Cause not stated	2		
Uræmia	1		
Exhaustion	1		
Anuria	2		
	11		
Deaths later		7	
(One year or under	6)		
Tubercular meningitis	1		
Tuberculosis of opposite kidney	2		
Pulmonary phthisis	2		
Cause not stated	1		
(Seven years	1)		
Tuberculosis of opposite kidney	1		
	7		
Improved (duration, a few months to five years; persistent pyuria complained of in all)		5	
Recoveries		13	
Duration not given	5		
One year or under	2		
Two years	3		
Four years	3		
	13	36	

We note that complete recovery may take place even if the ureter has been abandoned. On the other hand the mortality is quite large (50 per cent.), the deaths being either immediate (30 per cent.) or remote (20 per cent.). The cause of death in almost all the cases was tuberculosis in some form, suggesting, at least, that the tuberculosis of the ureter might have been the infecting centre. In one case such a result took place after a lapse of seven years. Among the ill results of abandoning the ureter are fistulæ, secondary abscess if the ureteral stump is buried, continuance and persistence of the pyuria. McCosh[1] reports the case of a man nephrectomized three years previously in whom a secondary abscess developed at the site of the ureteral stump. In another of his cases a secondary ureterectomy was required after nephrectomy, the ureter having become enlarged by a collection of pus within it. It is known, however, that a tuberculous ureter will sometimes atrophy. Brown[2] relates a case of a boy nephrectomized in whom the diseased ureter atrophied to a great extent; but the boy died seven months later of tuberculous meningitis, and at the autopsy tubercle bacilli were found in the ureter which had been abandoned.

To sum up, it appears that if the ureter is abandoned further complications may be expected, and the most to be dreaded is tuberculosis in some other part of the body. The excellent results obtained by

[1] Annals of Surgery, 1899, vol. xxix. p. 757. [2] Ibid., p. 755.

total and partial ureterectomy encourage the belief that it will be more commonly done in the future. It seems proper to insist that total nephro-ureterectomy should be done in all cases in which the condition of the patient warrants it. The added risk of the operation is very slight if the general condition is even fair.

There are some cases of ascending infection in which the ureter becomes progressively larger from below upward. In such cases the extension to the kidney is by actual growth of the disease along the course of the ureteral wall. The separated urines may show only a slight degree of pyuria on the affected side, but the diagnosis is easily made by the thickened ureter vaginally, the vesical appearances, and by finding the bacilli. The treatment of the case will depend on the extent of the ureter involved. If a small portion only is diseased it may be possible to divert the ureter into the summit of the bladder and excise the lower portion, including the ureteral eminence and possibly a portion of the bladder, depending on the extent of the disease.

GONORRHŒAL VULVOVAGINITIS IN CHILDREN.

By Richard F. Woods, A.M., M.D.,
of Philadelphia.

The severe results of vulvovaginitis in the young are of sufficient importance to warrant a more careful study of the character and mode of infection of this disease. I think it is practically certain from looking over the different series of cases reported, and from a careful study of my own, that most of these cases of vulvovaginitis are gonorrhœal in nature. I think, moreover, it is equally certain from these same collected cases that this disease in children is of much greater danger than is commonly supposed, and that the results are sometimes appalling. That the greatest care and thoughtfulness should be exercised with a vaginal discharge in children, both in regard to the local treatment, the care of the eyes, and infection to others, I am sure all who have had these cases to deal with will agree. The medico-legal aspect of the case also makes it of great importance. The knowledge which we have of the superstitious belief among the poorer classes, especially among the negroes, that connection or attempted rape with a virgin will cure the gonorrhœa in a male, made many, before the fact of the facility of contagion from other sources was known, jump at the conclusion of rape, and even now there is no more delicate or difficult medico-legal problem with which physicians are called on to deal.

The publications of Pott, von Duche, and Spaeth, which first placed the so-called vulvovaginitis of infants among the gonorrhœal affections, have been followed by reports of many cases, the large majority of which are gonorrhœal. In 1885 Fränkel in 62 cases which he examined with the microscope found diplococci which resembled in appearance the gonococcus of Neisser. Cseri also in 26 cases which he reported discovered a diplococci, which led him to think that all his cases were gonorrhœal in origin, although his cultures and inoculations were practically negative. Morse reports 21 cases, in 16 of which he was able to demonstrate the gonococci to his own satisfaction; and Cohenbrach found the gonococci in 20 out of 21 of his cases. Suchard reports 12 cases due to infection by towels, all of which he believes were gonorrhœal; while Weil believes that he traced 30 of his cases to infection from a rectal thermometer.

Skutsch's article is very interesting as showing how easily the infection may travel. He reports 160 cases of vulvovaginitis contracted by using the free baths at Posen. All the children had most of the symptoms of gonorrhœa, intense pain on urination, and in some of the cases there were marked constitutional symptoms. The bathing water was not changed frequently, and several children bathed together in the same tub. Dr. Steinschneider examined the discharge from 140 cases, and in 60 of them found gonococci. He came to the conclusion that all of the cases were gonorrhœal in origin.

In a large number of cases that Pott reported he considered that the origin of most of them was gonorrhœal; 1 in 8 of his cases had congenital syphilis, while only 3 in 86 cases followed attempts at rape.

O'Donavan makes the statement that in vulvovaginitis among negro children the slide invariably shows gonococci. Williams found the gonococci of Neisser in 4 out of 5 cases that he reports. Atkinson discovered 6 cases, all sleeping in the same dormitory, in an institution. Close questioning of some of the larger girls revealed the fact that they had been titillating the genitals of the smaller girls. In a year the institution was pervaded by a contagious ophthalmia. He comes to the conclusion that the vulvitis was caused by the ophthalmia, and not *vice versa*. Martin inoculated the pus from an infant, suffering from vulvovaginitis, into the urethra of a man; a severe gonorrhœal urethritis followed.

With such an array of testimony it would seem certain that the great majority of all cases of vulvovaginitis in children are of gonorrhœal origin. We must remember, however, that the mere finding of diplococci in the vaginal discharge is by no means positive. There is a great variety of diplococci in the vaginal secretion, as Bumm has shown; and while there is very little doubt, from the symptoms and

microscopic findings, of the gonorrhæal origin of most of the reported cases, still the doubt does remain until the gonococci in each case have been cultivated and inoculated.

In regard to the other causes of this disease, the following classification is, I think, sufficient:

Catarrhal.
  Filth.
  Exanthemata.
Traumatic.
  Rape.
  Masturbation.
  Mechanical injury.
Infectious.
  Oxyurides.
  Bacteria, pathogenic.

Atkinson lays down ulcerative stomatitis as a cause. Sheffield thinks that masturbation is a result more than a cause.

I can find very few cases where there was a coexistence of the oxyuris vermicularis, and none in which they have been definitely proven to have been the original cause. There is no doubt that they sometimes are the exciting cause, just as a scrofulous diathesis, filth, etc., may start the disease; but they are certainly rare compared to the gonorrhœal origin.

Gonorrhœal vulvovaginitis apparently can be contracted from towels, bathing vessels, sheets of the bed, etc., as has been shown from the cases above reported, the unprotected and prominent vulva in children seeming to be an easily accessible position for the inroads of the gonococci. Currier believes that an infant may be infected by its mother during parturition. This, I think, has occurred in the second case I report. Matin reports that a girl, aged six years, who contracted gonorrhœal ophthalmia from her older sister—with whom she slept and who was suffering from a vulvovaginitis—by sliding down on the sheets and getting the eye infected in this manner.

The microscope is the only means of telling the infectious from the non-infectious, and it is a good rule, as Williams suggests, to consider all cases infectious.

The symptoms seldom vary, and are generally typical. The vulva is bathed in a yellowish or whitish, thick discharge, which on pressure seems to exude from the vagina. The vulva and vagina in advanced cases are swollen, red, and painful on pressure. There is a slight rise in temperature, and constitutional symptoms sometimes are marked. Painful urination is not a constant symptom, although I think that the urethra is involved in infantile vulvovaginitis as often perhaps as in

gonorrhœa of the older women. In my Cases II. and IV. there was painful urination, although in Case II. it was rather uncertain. In Sheffield's table, out of 65 cases 13 presented severe symptoms of ardor urinæ. Cystitis is perhaps a rare symptom, although Cohenbrach, Comby, and Reblaud report it as a complication in some of their patients. Ophthalmia is the most common of all the complications. In Leszynsky's report, 18 children out of 35 contracted purulent ophthalmia. It occurred in none of my cases. Heart lesions are sometimes found accompanying vulvovaginitis, and arthritis, according to Storer, is quite common in the gonorrhœal form of this disease.

Hartly tells us of a patient of his—a girl, aged five years, suffering from a purulent vulvovaginitis—whose ankle became much swollen and presented all the appearances of gonorrhœal rheumatism. He also reports four other cases of rheumatism in children suffering from vulvovaginitis, and in one of these cases gonococci were found in the fluid from the joint.

The most severe and dangerous complication of infantile vulvovaginitis, however, is acute peritonitis, caused by the ascent of the infection up the uterus and tubes into the peritoneal cavity. Many cases of this kind have been reported. Stevens reports a case of a child, aged four years, suffering from a vaginal discharge, developing all the symptoms of acute peritonitis. The child soon went into collapse, and died. The leucorrhœal discharge he found by questioning to have been present for some time. Huber describes the case of a girl, aged seven years, who was suffering from a vaginal discharge; no microscopic examination was made. She developed symptoms of peritonitis. The diagnosis of ruptured appendix was made, but the operation revealed a normal appendix. There was general peritonitis, and the right tube was very much thickened and inflamed, evidently the channel by means of which the infection had travelled. He also saw a girl, aged eleven years, with an exquisitely tender and enlarged ovary and tube, who was suffering from a vaginal discharge. Sänger gives an instance of a girl, aged three years, who had peritonitis in consequence of gonorrhœal vulvovaginitis. Caille has seen a case, in an infant, aged five months, whose father was suffering from gonorrhœa. The child, who had ophthalmia and vulvovaginitis, finally developed peritonitis and died. There is very little question that in all these cases peritonitis was caused by the infection starting from the vulvovaginitis. Max found pus in the Fallopian tubes of children three times at autopsies. Sänger is perhaps right when he states that the cases of unexplained pelvic disease in virgins can be referred back to an infantile salpingitis that remained quiescent until puberty —an infantile salpingitis that owed its origin to a vulvovaginitis.

Sterility is in some women due to the same cause; and I think we will all agree with Currier when he says "it seems probable that many of the deformed and underdeveloped uteri with which are associated so much dysmenorrhœa, etc., are the consequence of infantile vulvovaginitis."

With all these complications and insidious sequelæ, how frightful the disease becomes. It is not merely a mild secretion which is caused by a cold or slight inflammation, and warranted to recover in a few days or weeks; it is a disease which bears grave and serious dangers, and should not be passed over lightly, but should be watched with the most faithful vigilance and precaution, and fought, step by step, until it is entirely eradicated and no doubt remains as to a complete cure.

In regard to treatment, I found the following very satisfactory in my cases: Cleanliness was enforced and proper hygiene attempted. The children were given small doses of quinine or syrup of the iodide of iron, three times daily. Strict attention was also paid to the bowels. Potassium permanganate was used in all the cases. A solution of 1:1200 to start with was used slowly through a rubber catheter; this was gradually increased until a strength of 1:2000 was reached. The douches were given twice daily, the genitals being thoroughly cleansed with soap and water before each treatment, and powdered boric acid was introduced into the vulva and blown into the vagina with a powder-blower after each douche.

Currier uses nitrate of silver, 2 per cent., in gonorrhœal forms. Storer advises that the infant of a gonorrhœal mother should have the genitals protected as well as its eyes, and should not be allowed to sleep with its mother. He thinks the greatest care should be taken to prevent ophthalmia, even to confining the hands; and the eyes, besides being washed with soap, should be washed in a bichloride of mercury solution every morning, as they are more liable to become affected during the night. Sheffield believes that the only preventive for ophthalmia is binding the eyes at night, and that nitrate of silver, 10 grains to the ounce, is an excellent abortive in the early stage of lacrymation. Pott advises bougies of iodoform; Pozzi, insufflation of iodoform; while Marfau uses bougies of alumnol, 2 per cent.

The histories of my own cases are as follows:

Case I.—M. F., aged three years. Three months ago her mother noticed a profuse discharge, which had caused a great deal of irritation and discomfort. The child's undergarments were constantly soiled and stained. Examination revealed the labia reddened and swollen, bathed in a white, thick discharge. There were no symptoms of infection of the urethra.

Case II.—H. C., aged three months. The child has a vulvovaginal discharge, which has been present since birth. The mother thinks that

urination gives the child some pain, as she cries when she performs the act. Vagina exudes a thick, yellowish discharge, which bathes the vulva. The mother was examined and found to have a vaginal discharge and some slight urethral discharge. The discharge of the mother was examined for gonococci, but none could be found. She admits that her husband suffered from gonorrhœa some time before her child was born, but is uncertain in regard to the date; moreover, she states that her labor was a very difficult one, and she thinks "that the child was born feet foremost." I think it is probable that it was a breech presentation, and that the child was infected at birth.

Case III.—A. W., aged eight years; has had a vulvar discharge for two weeks. Her symptoms and the examination were similar to the other cases.

Case IV.—M. W., aged ten years; is a sister of Case III. She has had a vulvovaginal discharge for three weeks. She has always slept with her younger sister. Both these children were brought to see me by the mother, who thought rape had been attempted. She thinks that her son, who is eighteen years of age, has gonorrhœa, but of this she is not positive. I think the elder girl was infected either by a utensil or a cloth of some kind, and in turn infected her sister, with whom she slept.

Case V.—F. H., aged four years; has suffered from vulvar discharge for three weeks; some pain on urination. The mother says that two weeks ago the child had inflamed eyes; when she presented the child for examination, however, there was no evidence of ophthalmia.

I will now state the results obtained from the cultures and the microscopic examination of these cases.

The test of the gonococci in the cultures is their growth on a medium of hydrocele fluid and agar and their refusal to grow on plain agar. This procedure was attempted in every case except one. How successful was the result the following will show:

In Case I. the discharge was stained with gentian violet. Diplococci were present, which were decolorized by Gram's solution. Cultures were attempted in agar and hydrocele fluid and a growth obtained. This was examined and found to contain diplococci, which were decolorized by Gram's method. A growth was obtained on agar, however, which makes the diagnosis uncertain. I still believe the gonococci to have been present mixed with some other organism, which developed on the plain agar.

In Case II. diplococci were found which were not typical. No growth was obtained on hydrocele agar. This case I consider negative.

In Cases III. and IV. the result was absolutely positive. Gonococci were found, which were decolorized by Gram's solution, and typical cultures were obtained on hydrocele agar, but no growths took place on plain agar. I consider both these cases to be gonorrhœal.

In Case V. examination of the discharge showed diplococci in the

cells, and they were decolorized by Gram's method. This patient was to return for a culture, but, unfortunately, disappointed us and remained away. Although the cultures were not obtained, I consider the case to be gonorrhœal in nature.

In consideration of the difficulty in growing gonococci and the liability of a mixed infection, I think the probability is that all the cases I report were suffering from gonorrhœal vulvovaginitis; however, the results obtained in the laboratory are the only positive ones, and show that out of five cases two were proven to have gonorrhœal vulvovaginitis, one was uncertain, one was negative, and in the other no culture was made.

I wish to express my thanks to Dr. Longcope, of the Ayer Laboratory of the Pennsylvania Hospital, for his kind assistance to me in my investigations.

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MEMOIR OF J. M. DA COSTA, M.D.

By Mary A. Clarke.[1]

Jacob Mendes Da Costa was born on the Island of St. Thomas, West Indies, on February 7, 1833. His father was John Mendes Da Costa, who lived at leisure as a gentleman of wealth in the West Indies, where his ancestors had been bankers and planters. His mother was a woman of great force and beauty of character. She was wise with a knowledge of the world, but had the simplicity and charm of a pure, tender-hearted, affectionate woman. The Da Costa family was an ancient one, of Spanish and Portuguese extraction. In the sixteenth century some of its members passed over into Holland, others settled in England, and through the English branch the subject of this sketch traced his descent.

The parents of Dr. Da Costa removed from the Island of St. Thomas when he was about four years of age. He remembered vividly a great conflagration that occurred shortly before this event, and could recall the ship on which they departed. For many years they resided in Europe, where careful attention was paid to the education of the children, largely by private instruction. Dr. Da Costa and his brother Charles were for three years at a gymnasium in Dresden, preparing for the University, and living under the care of old friends of their parents. On returning home, in 1849, a letter from these friends accompanied them, and an extract from this forms a pleasing picture of the two promising youths.

"Both return as you intrusted them to our care. Their hearts are as innocent and sincere as when they came to us. You will find their talents developed, their characters confirmed, their minds aspiring to everything that is good, right, true, and noble; their manners gentle and pleasing. Both are healthy and strong. As long as we shall live they will remain dear in our remembrance."

As a gymnasium student Dr. Da Costa devoted his time chiefly to the study of the classics and the modern languages, in which he became proficient, not only speaking French and German with perfect purity and great fluency, but acquiring, later, a reading knowledge of Spanish, Portuguese, Italian, and Dutch, while in the classics he was so thoroughly grounded that they remained always a source of delight. While in Dresden he worked very hard, and had no time to engage in sports such as are now in vogue among students. Except for lessons in fencing, dancing, and music, he knew little of recreation. During his

[1] For many years the private secretary of the late Dr. Da Costa.

youth financial reverses fell on the family, and on reaching manhood he had his way to make as many other young men.

Dr. Da Costa maintained, in after life, that he had no special talent for medicine. He thought that a man who succeeded in one career would have succeeded equally well in any other, hard work being the main factor, with something due to natural bent and favoring circumstances. In youth his tastes inclined him to politics or diplomacy; but friends dissuaded him, and he turned to the study of medicine, entering the Jefferson Medical College of Philadelphia in 1849, and graduating there in 1852, at the early age of nineteen years, his thesis being "Epithelial Tumors and Cancers of the Neck." In September, 1853, at the instance of Doctor, now Monsignor, Doane, he was made a Master of Arts of Burlington College, New Jersey.

After graduating in medicine Dr. Da Costa spent eighteen months in Paris and Vienna, pursuing chiefly the study of pathology and of internal medicine. While in Paris he lived in the Quartier Latin. He worked exceptionally hard, seizing the advantages offered by attendance at the various hospitals—l'Hôtel Dieu, la Charité, l'Hôpital des Cliniques, la Salpêtrière, Lourcine, and l'Hôpital du Midi. His favorite professors were Trousseau, Orfila, Nélaton, and Ricord. Early every morning he frequented the hospitals, attended private courses of all kinds during the day, and thus obtained special instruction from the internes and the young professors agrégés. He learned bandaging from the well-known and marvellously skilful "Père" Ribail, and also found time to take instruction in water-color painting.

His admirable knowledge of the language enabled him to make a far better use of his opportunities than was usual with American students. He enjoyed the drama, and eagerly sought by such means to enrich his store of choice and idiomatic French; and while acquiring the language he gained also an insight into the habits and customs of old Paris. In later life he loved to revisit the old book-stores on the quays, the restaurants, and even the same shops he had frequented when a student there.

In Vienna he was associated with August Klaatsch, the German physician and writer; and here he became the pupil and, indeed, the friend of Hyrtl, who presented to him a collection of microscopic specimens prepared by his own hands. These were subsequently given by Dr. Da Costa to the Biological Department of Columbia University, which had been endowed by his brother, the late Charles M. Da Costa.

In 1853 Dr. Da Costa returned to Philadelphia. He was soon appointed one of the physicians to the Dispensary attached to the Moyamensing House of Industry. He opened an office at No. 212 South Eleventh Street. Here he at once began the practice of medicine, and the instruction of students in physical diagnosis. These practical

classes in diagnosis were composed of ten or twelve young men—students and often graduates of medicine—and were exceedingly popular. There were three or four classes each year, and they were always filled in advance. Dr. Da Costa continued this mode of teaching until he became a lecturer on clinical medicine at the Jefferson Medical College. From such beginnings his practice grew slowly, but surely. It is true he passed through the usual dreary time awaiting its arrival, and he admitted having spent, like many another young doctor, a whole summer in the office of an absent physician, with little but thanks for the time and labor.

He early made investigations into the nature of yellow fever which called forth expressions of appreciation from René La Roche, at that time recognized as an authority in all pertaining to the disease. In 1854 he edited Kölliker's *Manual of Human Histology*, which had been translated by George Busk and Thomas Huxley. His paper, "Researches into the Nature of Typhus," was considered particularly valuable, and the young physician became known as a clear and brilliant writer as well as an original investigator.

In 1860 his class on diseases of the thoracic viscera passed a resolution of thanks, declaring they had ever found him "a courteous and accomplished gentleman; a zealous and skilful teacher; an eloquent lecturer, eminently accurate in all the attainments which mark the scientific physician."

When the *Medical Diagnosis* appeared, in 1864, it claimed the admiration of the medical world. It was the forerunner of other works of its kind, but has held its place during thirty-eight years. New works have appeared, some modelled on its lines, but none has rivalled it in scope, in teaching power, or in its matchless grace of composition. Competent critics have pronounced it to be the most elaborate work on diagnosis in the English language. Even in the library of the irregular practitioner it has an exalted place. As was stated by a journal of the day, in 1871, "Dr. Da Costa's *Diagnosis* will forever remain a monument to his ability, even though future labors were wanting to ornament and rear higher the shaft."

The book passed through successive editions, always in demand and always meeting the wants of the profession. The original plan was strictly adhered to, but new matter was constantly added, while the obsolete or that which had become untrustworthy was eliminated. The ninth edition was issued to the world just as its author was called away from this life. It had been delayed by the great fire that destroyed the building of the publishing company, and with it all the copies of the just printed book. Fortunately the advance sheets used for indexing had been preserved, and from these the reprinting went speedily forward. A proposition to condense the work and make it

conform to the limits of a text-book had been rejected, the writer preferring, when there should be no longer a demand for the work on its present lines, to let it go out of print entirely. The *Diagnosis* has been translated into German, Russian, and Italian, the German translation, issued in Berlin, having reached several editions, while French, Spanish, and Hungarian translations have been projected.

Dr. Da Costa became Visiting Physician to the Pennsylvania Hospital in 1865, and this association continued for thirty-five years. His love for the institution was a part of his life, and his character and labors added to its renown. With the lapse of years, honors and duties, one by one, were resigned, but to this he clung with never-failing affection and zeal. In 1897, at the opening of the Garrett Memorial building, in its splendid operating amphitheatre he delivered an address in which he reviewed the history of the beneficent institution and foreshadowed its perfection in the future.

At the close of the Spanish War the hospital became crowded with the soldiers brought from Porto Rico and the camps, and a call was made upon the staff for extra services. Dr. Da Costa came at once to the hot city and bore his part, personally examining forty or more typhoid cases daily. His treatment of these fever-stricken soldiers was attended with wonderfully good results, and he embodied his experience and observations in several papers, which he soon after published.[1]

In March, 1866, Dr. Da Costa became a lecturer on clinical medicine at the Jefferson Medical College, and in October, 1872, was elected Professor of the Theory and Practice of Medicine, succeeding to the Chair made vacant by the death of Professor Dickson. Here the most important work of his life was done, and his name must ever be inseparably connected with that of the institution. His fame as teacher, lecturer, and author travelled to distant countries and attracted pupils from everywhere to study under his guidance. Among his colleagues were the elder Gross and Pancoast, and near and far, in the great cities of the country and in remote hamlets, these three are spoken of by men who studied under them as "the great trio." In March, 1884, Jefferson conferred upon him the degree of Doctor of Laws.

The resignation of his professorship, in the spring of 1891, came as a surprise to many, and occasioned profound regret to his colleagues, and, in fact, to the whole profession. It was almost immediately after the delivery of a touching and powerful valedictory, which only one colleague knew was his farewell. The college, as soon as his resigna-

[1] Cases of Typhoid Cholecystitis Ending in Recovery, 1899; Phlegmasia Dolens in Typhoid Fever, Especially as Observed among Soldiers, 1899; Anomalous Eruptions in Typhoid Fever, 1899.

tion had been accepted, elected him Emeritus Professor, which position he held until his death.

As a teacher he felt that he had met with his greatest success in life. It has been stated that his public clinics were a feature in the medical progress of Philadelphia. Who can forget the magnetism of his teaching, the erect figure and calm face, the musical voice—slow, clear, yet sufficiently loud, and so graduated as to be heard by the entire audience? His style was simple, clear, and concise. The writer overheard one of his students say, at the conclusion of a lecture, "Da Costa always puts the thing in a nutshell." Even members of other professions delighted to be among his hearers, and a lawyer from a distant city admitted that it had been his habit for years to spend three days of every winter in Philadelphia in order to hear Dr. Da Costa lecture; yet, strange to say, few comments have appeared in print about his ability as a lecturer.

As a consultant he was ideal. Quick and keen in diagnosis, he was ever in sympathy with the perplexities and trials of the young practitioners. When he found them following a wrong diagnosis or erring in treatment, he gently admonished them in private, and thus enabled them to retain the confidence of the patient and family. Many doctors came to him in times of doubt or discouragement. From Maine to Oregon came letters and patients from the pupils who held him in affectionate remembrance.

Strange tales are told of his skill in diagnosis—one, often repeated, of a man being brought into the reception room of the hospital, where Dr. Da Costa, earnestly regarding him, declared him to be suffering from an abscess of the liver; looking again, still more earnestly, he pronounced him to have three abscesses, which proved to be the case.

During all these years he was writing, pamphlets and essays appearing in rapid succession—among them his paper "On Irritable Heart," which led to the general adoption of the name for this disorder; it was published in the *Medical Memoirs of the United States Sanitary Commission*, translated into German by Seitz, and issued in Berlin as a separate publication. Another was his Toner Lecture on "Strain and Overaction of the Heart," delivered before the Smithsonian Institution, in Washington, in 1874. Both were elaborate papers which presented a new view of the whole subject of diseases of the heart.

His work on *Inhalations* appeared in 1867. In 1878 he published *Harvey and His Discovery*, regarded by himself as his best production, but which failed to elicit general appreciation; this was republished, with notes, in a second edition. *Starvation Fever*, in 1880; *The Fluorides in Medicine* and *Nervous Symptoms in Lithæmia*, in 1881; *Pathology of Tubercle*, in 1882, and *Cocaine in Hay Fever*, in 1885, quickly followed.

"The Higher Professional Life," a valedictory delivered in 1883, is one of his most graceful compositions.

Two important essays were the Middleton-Goldsmith lecture, "Relation of the Diseases of the Kidneys, especially the Bright's Diseases, to Diseases of the Heart," delivered in 1888 before the New York Pathological Society; and, in 1893, "The Albuminuria and the Bright's Disease of Uric Acid and of Oxaluria"—a previously but little appreciated form of disease, which, in consequence, is now called by the name of "Morbus Da Costae." His lectures on "Cerebral Rheumatism," on "Valvular Diseases of the Heart," on "Malarial Paralysis," and that on "Lithæmia," delivered before the University of Pennsylvania in 1894, as well as his later papers—"Cardiac Asthenia," in 1894; "The Significance of Jaundice in Typhoid Fever," in 1898; "The Coexistence of Malaria and Typhoid"—have all given a deeper insight into these diseases, their causes, nature, and cure.

Among his most finished addresses—one teeming with noble thought and indicating profound research—was "The Scholar in Medicine," delivered before the Harvard Medical Alumni Association in 1897, at which time Harvard conferred upon him the degree of Doctor of Laws. In referring to Dr. Da Costa's attainments a journal of the day expressed the conviction that "Harvard voiced the universal sentiment of the physicians of America that this is the man whom we delight to honor. His work, teaching, example, and advice have done so much to advance the art and science of medical practice that no honor could be too great an acknowledgment."

Dr. Da Costa's work has been much quoted by other writers. Professor Friedrich examined carefully his essay on "Influence of Respiratory Percussion," verified it, and adopted it. Professor Jaccoud, too, made long extracts in his *Pathology* from the paper on "Researches in Typhus." Fagge, in his *Principles and Practice of Medicine*, refers at length to the paper on "Irritable Heart."

Upon Commencement Day, 1892, Dr. Da Costa received from the University of Pennsylvania the honorary degree of Doctor of Laws; and at the bestowal of the degree, in acknowledgment, he happily responded, "Tibi prefecto insigni, et Universitati celeberrinae, cujus fama, te agendo, ubique per terras augetur, ex imo pectore, gratias do." In February, 1899, he was made a Trustee of the institution. During the last year of his life he was much engaged with the proposed changes in the Medical Department, and he became one of the founders of a retiring fund for professors.

Dr. Da Costa always felt a lively interest in military matters. During the Civil War he was made Acting Assistant Surgeon of the United States Army and assigned to duty at the military hospital at Sixteenth and Filbert Streets, Philadelphia. Here he gathered much of the

material for his paper on "Irritable Heart." In 1892 he became a member of the Military Service Institution of the United States, and read its journals regularly. In 1896 he delivered an address of welcome to the Association of Military Surgeons, then assembled in Philadelphia, which evidenced an intimate knowledge of the changes in modern warfare, and was a beautiful tribute to the gallantry and devotion of the medical men whose names are illustrious in the annals of war.

He always took pride in his connection with the College of Physicians of Philadelphia, one of the oldest and most influential medical societies in America, of which he became a member in 1858, and of which he was twice President, serving from 1884 to 1886, and again from 1895 to 1898. He loved this ancient institution with undiminished affection until the last hour of his life. Its motto, "Non sibi sed toti," as he so fitly said in an address in 1885, encouraged its sons not to rest until they had permanently enriched the science for which they were banded together. He believed, with Rush, that if the College continued as discreet as it should be in the admission of members its fellowship would become in time "not only a sign of ability, but an introduction to business and reputation in physic." On this occasion he expressed the opinion that the College itself was at fault for not being rightly known to the public nor sufficiently appreciated, the College being inclined to keep within itself and to refrain from speaking publicly on the medical questions of the day—questions concerning which its members were best qualified to speak with the voice of authority. He felt that the advantages of membership in this institution were great, and was anxious that its high standards should be maintained, but thought there should be greater liberality as regards admission, and he urged a reduction in the annual fees, claiming that no young man of ability, lacking in means, should, for the want of money, be debarred association with a society conferring such benefits. During his last presidency he made a strong plea for increasing the number of members. He proved by painstaking research that the proportion of members to the number of doctors in the community was greater one hundred years before, as shown exactly by the *City Directory* of 1796, than at the present time.

Between his two terms of office, when it was feared that the epidemic of cholera then prevailing in some parts of Europe might extend to our shores, he was appointed chairman of a committee of the College to devise ways and means of meeting the emergency. Toward the close of his last term an epidemic of typhoid and our infected water supply caused him great anxiety. He wrote to the Mayor, urging filtration as the most speedy remedy, leaving for future discus-

sion the question of a new source in the Delaware water-shed rather than the Schuylkill.

He was much concerned, too, by rumors of the proposed measure to make the competitive hospital appointments of Philadelphia open only to residents of the city. He deprecated this as a step in a backward direction, and thought it would ruin Philadelphia as a medical centre by removing one of the incentives to young men in all parts of the country to come here for their studies.

In the President's address of 1895 he expressed regret that the valuable papers presented at the meetings of the various sections throughout the year could not be fully published, and he suggested ways of arranging for this in the future. That he had the progressive movement much in mind is shown by provisions in his will.

Dr. Da Costa was greatly opposed to the publication of biographical sketches of the living, and invariably refused to give information concerning himself for such projected works. Only after Harvard had conferred upon him, in 1897, the degree of LL.D., and at the urgent request of the editors of the *Harvard Graduates' Magazine*, he furnished them a brief sketch of his life, which has been made use of by other journals.

Tributes to his medical skill had not been wanting. Besides the associations which continued throughout his life he had been Attending Physician to the Protestant Episcopal Hospital and to the Philadelphia Hospital, and Consulting Physician to the Children's Hospital. He had been a member of the American Medical Association and also of the Pathological Society of Philadelphia, of which he was once the President. He had also been President of the Association of American Physicians, an honorary member of the Medical Society of the State of New York, a corresponding member of the Pathological Society of New York, and a member of the Medical Society of London.

After caring for the eminent British surgeon, G. W. Callender, of London, who fell ill while travelling in this country, Dr. Da Costa received very complimentary resolutions of thanks from St. Bartholomew's Hospital.

Social and scientific honors came to him from all sources. In February, 1852, he became a member of the Academy of Natural Sciences of Philadelphia. In 1855 he was made a member of the American Academy of Arts and Sciences of Boston; in October, 1866, of the American Philosophical Society; in 1867, of the New England Historic and Genealogical Society; in 1890, of the Trinity Historical Society. He joined the Contemporary Club in 1888, and was one of the original members of the Mahogany Tree Club, which was organized, in 1889, by the late Dr. William Pepper, and had among its

members the late Hon. Thomas F. Bayard, Dr. S. Weir Mitchell, Daniel C. Gilman, Professors Langley and McMaster, and the late Frank Thomson.

In his brief leisure Dr. Da Costa loved to dispense an easy hospitality, and his beautiful home at 1700 Walnut Street received not only the friends he loved, but occasionally strangers of distinction who brought him letters from his friends abroad. In 1888 he became a member of the famous Wistar Association, inaugurated by Caspar Wistar in 1800, "when Philadelphia bore the palm in literature and society." In this association Dr. Da Costa seemed to transmit the traditions and memory of the founder himself, and formed a connecting link between the leaders of medicine and the representatives of other professions in the city. Like Wistar, he was "an admirer of happy human faces."

The meetings were always held on Saturday night, and it was a custom to invite any eligible sojourners who happened to be in the city. On one of these occasions Emil Pasha, the African explorer, was a guest; on another the late Duke of Buckingham, as was also Sir Henry Stafford Northcote, the present Governor of Bombay. Dr. Da Costa resigned from the Association in 1898, feeling it a duty to make way for a more active member.

For years it had been generally understood that Dr. Da Costa was "at home" to receive any friends on Sunday evenings, and this gave opportunity to many to enjoy his society as well as to meet the cultivated and eminent men of the city—writers of distinction, famous jurists, men of science, artists, and explorers. They entertained each other, and had simple refreshments of wine and cigars.

Another association that gave him unmixed pleasure was that of the Shakespeare Society. He attended the annual dinners, and greatly enjoyed the toasts, with their apt Shakespearean accompaniments. At the last dinner, in April, 1900, an innovation was the taking of a picture of the festive board; but, unfortunately, the only face in the goodly company not distinctly shown by the artist was the one so soon to become only a memory.

Books were his friends. With a wide knowledge of general literature he retained his early love for the classics. His great success as an author was due to his profound knowledge of the best authors. The gathering of his miscellaneous library gave him keen pleasure, and it embraced few books which he had not read. It contained many memoirs of distinguished men, illustrating the best of the times. It was especially rich in the English classics, always in choice editions and appropriately bound. For its size it was probably one of the best selected libraries of English literature ever gotten together.

Dr. Da Costa's admiration of Thackeray was unbounded, and his collection of first editions of this favorite author was an almost com-

plete one, as was also his collection of the writings of Sir Arthur Helps.

He never enjoyed reading a book from a library. He might read one loaned by a friend, but to thoroughly enjoy a book it must be his own. Rarely did a summer pass without his reading over again some of the favorites of his youth, such as the novels of Sir Walter Scott or Cooper, and the works of Kipling and Marryat gave him pleasure. Tales that ended tragically were an abhorrence to him, and to these he infinitely preferred the subtle frivolities of Anthony Hope.

He disliked, in writing, all compound words, as well as interjections, of which he never made use. A purist in language, he loved all that was pure and best in literature. Slang was most repugnant to him. A coarse expression gave him positive pain.

He was abstemious in habit, a small eater, an early riser, given to punctuality. He would not lie on a couch to rest, but rested always in a big chair. During his student days in Paris early rising had become a necessity and fixed habit, which clung to him through life. In the summer of 1898, in the hours before breakfast, he amused himself by translating a Latin ode, "To Sestius," which was published in a university magazine. Even in his latest years much of the literary work he accomplished was performed in these early hours. He had, too, the invaluable habit of utilizing the minutes. Important letters were dictated in the few moments of waiting for his carriage or in the brief intervals between seeing patients.

Dr. Da Costa's personality was charming; his grace of manner such as is rarely seen, and can never be forgotten. His kindness of heart made it impossible for him to cherish resentment. The calls upon him for aid, from people known and unknown to him, were numberless, and it was most difficult for him to turn a deaf ear to these petitions. He believed it unwise to lend money, but thought it better to give outright the help desired. It caused him keen distress to remember that he had been unkind or hasty in speech, or had denied a request that might have been granted; and sometimes, when he had turned strangers away, laborious efforts were afterward made, as the writer well knows, to find them and give the help at first refused. It really grieved him to know that a little colored newsboy, who daily presented papers for sale as he entered his carriage, had been driven away from the corner by an over-zealous policeman.

The familiar little tin sign, loosely placed in the window and simply inscribed "Dr. Da Costa," was the only one he ever had. In the last year of his life this frequently fell out of the window, being returned to the house by small boys, who regarded it as of great value, and who, by Dr. Da Costa's orders, were rewarded for restoring it. Prob-

ably from its falls it had acquired a worn appearance, and Dr. Da Costa remarked, one morning, in April, "The sign has done its work, and the owner, too; we will soon be gone together."

Dr. Da Costa sometimes asserted that he ought not to have been a physician; he felt too much distress at the sufferings he witnessed, and this distress grew upon him with advancing years. In his last address before the Jefferson Medical College he mentions a Nestor in the profession who could neither eat nor sleep when contending with a dangerous malady, and no one can doubt that this statement was true of himself.

His professional manner was quiet and gentle. His attention was never distracted, and the patient and friends were always impressed by the fact that, for the time being, the case absorbed him. Before leaving the sick-room his last words were addressed directly to the patient, and conveyed to him some comforting thought.

Dr. Da Costa was a regular attendant of the Protestant Episcopal Church, and lived the life of a sincere and devout Christian. No pressure of work was allowed to interfere with his daily reading of the Bible, and on Sundays much of his time was passed in its close study, with the aid of the best commentaries to be obtained. The books of Job and Isaiah and the Pauline epistles were his favorite portions. The hymns he loved best were "Lead, Kindly Light," and "Nearer, My God, to Thee," and these, as he had requested, were sung at his funeral.

In 1860 Dr. Da Costa married Miss Sarah Frederica Brinton, daughter of the late George Brinton and sister of Professor John H. Brinton, a colleague and lifelong friend. After a protracted illness Mrs. Da Costa died in 1889, leaving one child, Charles Frederick, now a member of the Philadelphia Bar.

Dr. Da Costa's last address, "Questions of the Day in Medicine," delivered before Yale University at the end of June, 1900, occasioned general comment in this country and in Europe. It was a powerful plea for the amelioration of the condition of the poor consumptive, and reawakened interest in these hapless creatures. He endeavored to prove conclusively that consumption—so familiar to us all, and viewed with stolid fatalism—is more destructive to human life than epidemics of cholera or yellow fever, because more continuous and widespread. He begged that legislation be brought about to provide sanitaria for the cure of the disease, and indicated that in this cause our merchant princes might find an outlet for their most abundant philanthropy.

Dr. Da Costa had never been strong after an attack of influenza in 1890. A severe illness in the autumn of 1894 still further impaired his strength, though he apparently recovered, and was benefited by a

sojourn at Carlsbad in 1895 and again in 1896. During one of these trips to Europe he visited Edinburgh for the first time. Professional men in England and Scotland welcomed him warmly as one of the foremost of American physicians, and on the Continent the same cordial hospitality was shown to him. In Berlin he was entertained by Professor Leyden, the court physician, recently returned from attendance on the late Czar of Russia.

While he had passed many years in Europe, he had never seen Rome, and he greatly desired to go there as well as to visit Greece and Spain. He felt, too, that a warm climate would be beneficial to his health, but the time for giving up his practice never came. On the day of his death he again expressed a wish to see Rome, but added, "I have made no arrangements, and therefore cannot go this year, and next year I shall not be here."

This premonition of death seemed to be with him for several months. In the spring of 1900 he told his secretary that he believed he should not live a year, and thereafter he made the assertion frequently. He felt no fear of death, but hoped he should not suffer much. For three years he had been subject to attacks of pain on taking exercise, and in June, after an attack of unusual severity, with great oppression, he expressed a conviction that the cause was angina pectoris. In the following August, when alone in Boston, he had another violent seizure, but he mentioned it so lightly to those nearest him that none was aware of the serious nature of his malady.

When the end came, with terrible swiftness, at the close of a day of great activity, the blow to all who loved him was of crushing force. He had dreaded a life of invalidism, but this he was mercifully spared. He died at his country-seat at Villanova, Pennsylvania, September 11, 1900.

In closing this short sketch of a beautiful and noble life, no words seem more fitting and appropriate than those breathed by the prophet Micah of old: "He hath showed thee, O man, what is good; and what doth the Lord require of thee, but to do justly, and to love mercy, and to walk humbly with thy God."

REVIEWS.

A Treatise on Diseases of the Skin. For the Use of Advanced Students and Practitioners. By Henry W. Stelwagon, M.D., Ph.D., Clinical Professor of Dermatology, Jefferson Medical College and Woman's Medical College, Philadelphia; Dermatologist to the Howard and Philadelphia Hospitals. In one octavo volume of 1125 pages, with 220 text illustrations and 26 full-page lithographic and half-tone plates. Philadelphia and London: W. B. Saunders & Co., 1902.

The avowed purpose of the author in writing this book was to produce a practical treatise upon dermatology which should be useful to the general practitioner as a guide in the recognition and treatment of diseases of the skin as seen in his daily practice, and a careful survey of this imposing volume of more than a thousand pages has convinced us that he has performed his difficult task with more than ordinary success. While the scientific portion of the subject is by no means neglected, etiology and pathology being given due consideration, the more practical matters of diagnosis and treatment are especially emphasized and treated at great length. As being the very alphabet of diagnosis, the primary and secondary lesions of diseases of the skin are described with unusual care. The section upon General Diagnosis seems to us especially worthy of notice as containing many useful hints upon the recognition of cutaneous diseases; it well repays reading. We note that special importance is attributed to the distribution of cutaneous eruptions as affording very valuable aid in diagnosis, a point which is not sufficiently emphasized in many text-books. We also observe that the author is not inclined to attach too much importance to the history of cases as obtained from the patient, believing that it is often misleading; and this is in entire accord with our own experience, which has convinced us that the history as ordinarily given is just as likely to lead away from as toward a correct diagnosis. Indeed, we have long felt that errors will frequently be avoided by relying upon the objective symptoms alone, disregarding the history. In the sections devoted to treatment the numerous remedies useful in the various diseases are not merely enumerated, as is sometimes the case, but a wealth of detail is given as to the manner of employing them—a matter of quite as much importance as the selection of the remedies themselves.

On account of the absence of any entirely satisfactory classification of diseases of the skin, the author was at first inclined to go around the difficulty by adopting the alphabetical arrangement provisionally used by the American Dermatological Association and employed in a number of the more recent text-books, notably those of French authorship; but upon due reflection he concluded that some system of classification, even though imperfect, was desirable for teaching purposes, and adopted the well-known pathologico-anatomical system of Hebra as modified by

more recent authors. This system, although admittedly open to criticism at many points, is, perhaps, in the present state of our knowledge, the most practical yet devised. The ideal scientific system would be one based upon etiology, but the gaps in our knowledge of the causes of disease are yet too many and too wide to make such a system practicable; but it is not too much to hope that the present enormous activity in every department of medical research will, in the near future, make possible a reasonably successful attempt at such a classification.

Eczema is held to be a catarrhal inflammation of the skin, due to a great variety of causes, internal and external. The micro-organisms present are not believed to bear any pathogenetic relation to the primary lesions of the disease. We are glad to notice that the term "parasitic eczema," employed by some authors to designate those forms of the affection characterized by rounded marginate patches, finds no favor. It is considered a "vague term;" we would go further and say that it is quite indefensible, since no special organism has yet been demonstrated in these cases; and without such demonstration the use of the term is without warrant. The term tuberculous as applied to the eczemas occurring about the mouth, eyes, ears, and nose in strumous children is also believed by the author to be used without sufficient foundation. Treatment is considered at length, and the safe middle ground is taken that, for the successful management of this extremely frequent and very important disease, both constitutional and local remedies are necessary. The section upon Constitutional Treatment begins with the statement that this does not mean the employment of drugs alone, but includes the regulation of the diet and all other hygienic measures which conduce to the patient's health, a statement which we commend to the thoughtful consideration of the young practitioner and some old ones as well. It is pointed out that there are no specifics for eczema, and that the internal treatment must be carefully adapted to the individual case. Among many other local remedies, the gelatin preparations, as recommended by Pick, Unna, and others, are considered of great value.

All the forms of impetigo are stated to be contagious, and the several clinical varieties are described under the one title, impetigo contagiosa, the author believing that, while not scientifically exact, this manner of treating the subject is the most practical. The view that the affection is due, in most cases, to ordinary pus cocci is accepted, although it is also stated that other micro-organisms may occasionally give rise to it. We do not believe that future investigation will confirm this view; we believe the disease will be found to be due to a special micro-organism.

In no class of affections is the tremendous advance of our knowledge of the etiology and pathology of cutaneous diseases in the past two decades more apparent than in the tuberculoses of the skin. Picking up the last edition, published twenty years ago, of what was by common consent the best text-book upon diseases of the skin in the English language at that time, we find a half-page given to tuberculosis of the skin. In this treatise no less than forty pages are devoted to this most important subject. The considerable number of eruptions known as scrofulodermata at last here find their proper place after having been treated so long as maladies due to a peculiar indefinable something called struma.

We are glad to see that some account, even though brief, is given in

a supplementary section, of some of the commoner diseases of the mucous membranes adjoining the skin. We have long thought that text-books upon dermatology should include a description of those diseases of the mucous membranes which are associated in a certain proportion of cases with cutaneous eruptions, as well as of those independent affections which are most apt to come under the observation of the dermatologist.

To the specialist in diseases of the skin one of the most valuable features of the book is the abundant references to dermatological literature which appear on every page. These must prove of great value to every worker in this field of medicine, and ought to insure the volume a place in the library of every student of dermatology.

This review would be glaringly incomplete without some reference to the beautiful illustrations which abound throughout the volume. These consist of reproductions of photographs and colored plates. The former are especially deserving of notice, since they are, with but few exceptions, unusually fine, and add much to the value of the treatise as a text-book.

In conclusion, we believe this to be one of the best books upon the subject in the language, a clear, practical exposition of dermatology as it exists to-day. M. B. H.

A Manual of Surgical Treatment. By Watson Cheyne, M.B., F.R.C.S., F.R.S., Professor of Surgery in King's College, London, and F. F. Burghard, M.D., M.S., F.R.C.S., Teacher of Practical Surgery in King's College, London. Vol. VI. Philadelphia and New York: Lea Brothers & Co.

In this the sixth volume of the *Manual of Surgical Treatment*, Cheyne and Burghard discuss the surgery of the tongue and floor of the mouth, the pharynx, the neck, and the œsophagus, and also some of the surgical diseases of the abdomen. It is important to note that they entirely condemn the division of the frænum, so often practised on infants for tongue-tie. They say that in the majority of cases such an operation is unnecessary, because the frænum lengthens as the child advances in years; and besides this, the operation may be followed by a scar, which anchors the tip of the tongue. When it is absolutely necessary to divide it, they make a transverse slit close to the symphysis of the jaw, pull up the tip of the organ, and thus convert the transverse cut into a lozenge-shaped area; and they put two fine catgut stitches between the lateral angles of the lozenge, so as to prevent the formation of a broad granulating surface.

The chapter on Cancer of the Tongue is admirable, and many important facts of which the authors have themselves made a careful study are pointed out. It is an interesting fact that in cancer of the tongue, whereas the lymphatic glands beneath the jaw soon become involved, the lymphatic vessels themselves are not involved to anything like the extent that the lymph tract between the axilla and the breast is involved in cancer of the breast. Large cancer cells travel through the lymphatics from the tongue to the neck without being arrested on the way, and the lymph tract between the tongue and the glands is affected

only in advanced cases. This leads us to the important conclusion that it is not always necessary to remove the structure between the tongue and the glands; in other words, it is not always necessary to cause the wound in the mouth to join that in the neck. In the early stages it is safe to leave this lymphatic tract untouched. Theoretically, it would be best to remove the fat and glands from the anterior triangle, as is done with those from the axilla in cancer of the breast, even when no lymphatic involvement can be detected by palpation. The authors show us, however, that there are certain disadvantages in doing this. The lymphatic area is not well defined and is very extensive; the infection may extend in many different directions; the glands, when enlarged, can be removed only with difficulty; and it is very hard to clear the region of all fat glands when the latter are not definitely enlarged, some glands being almost certain to escape. If, however, the triangles are once opened, an attempt should be made to remove all the glands then; for it will be practically impossible to do it at a secondary operation, because the scar-tissue will so distort the parts and mat the structures together. The authors think it is better to open the triangles only when there is a certain amount of glandular enlargement present, because this enlargement acts as a sort of guide. If no detectable glandular enlargement is present, they simply remove the disease from the mouth, recognizing that the glands will become involved sooner or later, and may be removed as soon as they do become obviously involved.

The section on the Examination of the Stomach Contents is also very thorough. In performing gastrostomy the authors prefer Witzel's operation. In the chapter on Ulcer of the Stomach they say that the indications for surgical treatment in that condition are the following: (1) When the symptoms have lasted long and do not yield to medical treatment, especially when marked anæmia is resulting from repeated hemorrhages; (2) to arrest profuse hemorrhage that threatens life; (3) to relieve pyloric constriction or hour-glass contraction, and thus cure dilated stomach; (4) when perforation occurs; (5) to relieve indefinite symptoms due to adhesions; (6) to treat a subphrenic abscess.

The various operations are described in detail. The authors recognize the value of the Murphy button; but, nevertheless, they would employ it only in cases of great urgency in which the condition of the patient does not warrant the simple suture operation. They do not think favorably of complete gastrectomy, believing that when a cancer involves a large part of the stomach the neighboring glands will be extensively infected, and other structures adhering to the stomach will be involved; and they doubt whether it is wise to attempt this radical procedure.

The authors then proceed to discuss intestinal obstruction, intussusception, appendicitis, hernia, etc. They are somewhat conservative in some of their views upon the surgical treatment of appendicitis as is common among our English confrères. They believe that when an appendicial abscess is operated upon it should be allowed to heal; and after healing is complete, unless the appendix has certainly sloughed off or has been gotten rid of when the abscess was opened, an operation should be performed for its removal. When several attacks of typical relapsing appendicitis have occurred the appendix should certainly be removed. Even in mild cases of relapsing catarrhal appendicitis the appendix should be removed. If the patient has only one mild attack of catarrhal appendicitis the authors do not advocate subsequent

removal; but when the attack has been severe, they do advocate it. Cases of so-called appendicular colic demand operation. In fulminating and perforating cases, operation should be performed at once, without a moment's delay. When there is suppuration the authors believe that there is distinct risk in waiting for an abscess to extend to the anterior abdominal wall; they maintain that the sooner the abscess is opened, the better. In abscess cases they content themselves with opening the abscess; they do not make any attempt to remove the appendix then, while the infection is virulent and acute, rather preferring to remove it later, after healing has occurred. They say, however, that they cannot help regarding operation during an acute attack, when there is no definite reason for believing that pus is present, with a certain amount of hesitation. If a surgeon is called to a case of relapsing appendicitis within a few hours of the onset of an attack the authors advocate operating at once, because at this time the micro-organisms are still within the appendix and have not penetrated the peritoneal cavity, and the operative manipulations need not diffuse septic material through the peritoneum. After twenty-four hours, however, there is inflammation of the surrounding peritoneum and bacteria have begun to go into the peritoneal cavity. If left alone, these are likely to remain limited to the appendix region; but if the adhesions be torn through they may be diffused and cause general peritonitis. If the favorable moment for operation has passed, the authors are inclined to delay, carefully watching the patient while they wait. They believe that a careful and repeated blood count is of great importance in telling when suppuration begins.

This volume is filled with practical articles. The descriptions of conditions is terse and accurate. The directions for treatment are positive and concise. It is not a compilation, but represents the matured views of two surgeons of extensive experience. It is a worthy companion volume to its predecessors. J. C. Da C.

A Treatise on the Diseases of the Throat and Nose and Associated Affections of the Ear. By Charles P. Grayson, M.D., Lecturer on and Instructor in Laryngology in the Medical Department, University of Pennsylvania. Octavo, 540 pages, with 129 engravings and 8 colored plates. Philadelphia and New York: Lea Brothers & Co., 1902.

The author of this work has had such lengthy experience as a teacher on this subject in one of the great medical colleges of this country that it is *prima facie* evidence of his qualifications to write a student's text-book. The book itself bears out this by its intrinsic adaptability to the needs of students. All such works at the present time must be more or less a rehash of previous books. Dr. Grayson's shows much more originality than the average. The author has constantly kept before him the fact that it is for the student that he primarily writes; consequently the description of the appliances needed for work in the nose, throat, and ear is limited to those things which are absolutely necessary, and we are not treated with a long series of "the author's modifications" of various simple instruments, and the same is true in his account of operative procedures.

The very qualities which render the book of value to the student also open it to the only adverse criticism which we find ourselves called upon to make; namely, it has necessitated the elimination by the author of discussions of some of the most interesting but intricate problems of laryngology and otology. Thus, diseases of the accessory sinuses are dismissed with a very few paragraphs. Mycosis of the tonsils is attributed to the lepothrix, no mention being made of the recent studies by Richardson, Kyle, and others, which have proven that this condition is in most instances not due to the leptothrix but a true keratosis. The author deprecates the use of the galvanocautery in most instances.

One statement which will carry comfort to many but conviction to few is that hay fever is a curable disease. It may be curable, but in the opinion of many of the profession and most of its victims the cure is only to be found by repeated sojourns in a suitable climate during the season in which the victim suffers. The author, in justly ironical language, refers to the recent promulgation of the "discovery" of the value by internal administration of a preparation of the plants which usually produce hay fever, for the purpose of its cure.

A most attractive feature of the book is found in the style in which it is written and in its author's well-chosen language. The book cannot be too highly commended for the use of students or of beginners in rhinology and otology. F. R. P.

A Treatise on Massage: Its History, Mode of Application, and Effects. By Douglas Graham, M.D., Member of the American Association for the Advancement of Science; of the American Medical Association; of the Massachusetts Medical Society, etc. Third edition, revised, enlarged, and illustrated. Pp. 462. Philadelphia and London: J. B. Lippincott Company, 1902.

Taschenbuch der Massage für Studirende und Aerzte. Von Dr. Erich Ekgren, an der III. medicinischen Universitätsklinik zu Berlin, S. 90. Berlin: S. Karger, 1903.

A Pocketbook on Massage.

Nearly twenty years ago we read in its first edition the treatise which comes before us for criticism and review. At that time we were impressed by the honesty and frankness of the author in deducing its indications and contraindications based on the results of its application on over fourteen hundred patients. The present is practically a new work in its scope, in its basis, and in its development. Matters are here presented which have come into medical knowledge and literature, but were then undreamed of; for instance, the neuroses. Physiology has made giant strides; so also has chemistry. Anatomical facts have received new interpretations. The author is no longer solitary as a medical practitioner practising massage and asking for its recognition as manual therapeutics, an ethical, logical, even if ill-understood and underestimated branch of general therapeutics. He is in good company, with broad-minded, well-informed physicians who write on, advise, and practice massage. If his language at times is not that of argument, we may assume that its pungency is developed because the non-

academic statement failed to arouse intelligent interest. Even if his treatment of the subject is strongly *ex parte*, can we expect that any other position would command the attention of his readers? When the author stops short of extravagant claims and recognizes the limitations of his method, as he does, we must acknowledge the strength of his argument. We have taken no trouble in reading the book, for in its perusal from militant preface to prosy index we have found profit in every page, amusement in some chapters, and occasionally an arousing of our curiosity. The illustrations are particularly good, especially those which are borrowed to point out how massage should not be performed. As the dedication has grown from one individual of the first to his "old professors" of the third edition, so we trust that the author's audience will be increased in geometrical progression. As a thoroughly readable work, written by one whose extensive research and long practice, tempered by judicial reasoning, entitle him to a hearing from progressive practitioners, we add our hearty commendation.

The little book of Ekgren opens with a preface by Senator, recommending not only massage but the author as its exponent. It can readily be carried in the pocket, although its contents are none too deep or extensive for the head of an average practitioner. So far as it goes it is excellent, and will, we trust, excite a desire on the part of the reader to acquire the information found in more complete works.

R. W. W.

MORPHINISM AND NARCOMANIA FROM OPIUM, COCAINE, ETHER, CHLORAL, CHLOROFORM, AND OTHER NARCOTIC DRUGS; ALSO, THEIR ETIOLOGY, TREATMENT, AND MEDICO-LEGAL RELATIONS. By T. D. CROTHERS, M.D., Superintendent of Walnut Lodge Hospital, Connecticut; Professor of Mental and Nervous Diseases, New York School of Clinical Medicine, etc. 12mo., 351 pages. Philadelphia and London: W. B. Saunders & Co., 1902.

THE author states that the special object of his book is to bring the subject (of drug habits) out from its present empirical stage to higher and more scientific levels, and to encourage further and more exhaustive studies. As a matter of fact, it is rather a popular exposition of drug habits and the methods of treating them. The greatest space is, of course, given to opium and morphine—269 pages out of 344. Dr. Crothers is more pessimistic as to the frequency of morphinism than many authorities, claiming, for example, that 10 per cent. of something over three thousand physicians were victims. If this holds true of all the physicians in the country, a temperance crusade is much needed. The author exaggerates a little in the chapter on Tobacco, at least we who use tobacco think so. To say unconditionally that the use of tobacco is not only dangerous but certain to be followed by debility, mental perversion, and exhaustion is to use very strong language. He also says that oculists describe tobacco amblyopia as very common. The oculists of our acquaintance are of opinion that it is not very common, and, indeed, very rare save in drinkers. Finally, it appears that there is some question as to moral and mental responsibilities of tobacco habitués. Surely the doctor is a little radical, but withal he has written an interesting and useful book.

C. W. B.

A Practical Treatise on Smallpox. By George Henry Fox, A.M., M.D., Consulting Dermatologist to the Health Department of New York City, with the collaboration of S. D. Hubbard, M.D., S. Pollitzer, M.D., and J. H. Huddleston, M.D. Illustrated by colored photographs from life. Philadelphia and London: J. B. Lippincott Co., 1902.

Well-made photographs of properly selected subjects render most valuable aid in the recognition of many cutaneous affections; indeed, in many cases they are more instructive than pages of the best text.

In this treatise an attempt is made to present by the aid of photography one of the most important of the eruptive diseases. In a series of fifteen plates, reproductions from photographs from life, the various eruptive stages of variola are presented, while a sixteenth is devoted to vaccination and varicella. Most of the portraits are colored, which—as a rule, to which, however, there are some exceptions—adds to their realistic appearance. Those representing the vesicular and pustular stages are beautiful examples of what photography is capable of in the way of accurate representations of cutaneous eruptions; it would be difficult, indeed, to improve upon them. But the photographs of the earliest stages of the disease are much less satisfactory, not through any lack of skill in the photographer, but because of the unfortunate limits of photography, the erythematous and papular lesions present at this period of the disease not lending themselves well to photographic reproduction. This is the more to be regretted because it is just in the early days of the malady that doubt and error in diagnosis are most apt to arise.

The text, which is intended to be practical rather than exhaustive, is clear and concise, the section of diagnosis being especially so. The occurrence of the lesions of smallpox on the palms and soles is especially emphasized as an important diagnostic symptom.

Although the very best illustrations possible will always be found inadequate substitutes for bedside experience, yet plates such as these are sure to be of great service to the inexperienced who have not had the opportunity to study smallpox in the living subject, and to these this illustrated treatise is heartily recommended. M. B. H.

The Healing of Nerves. By Charles A. Ballance, M.S., F.R.C.S., and Purvis Stewart, M.A., M.D., M.R.C.P. Illustrated by 16 plates and 1 figure in the text. London: Macmillan & Co.

This book is based on experimental sectioning of nerve trunks in monkeys, dogs, and cats, and on a study of nerves obtained during operations on human beings for the relief of injuries. The problem the authors consider is the process of degeneration and regeneration in a peripheral nerve after injury, with and without immediate or late suture, and the changes which occur in nerve grafts. The question is one of great scientific interest, and the carefully conducted experiments detailed by the authors go far to prove that the theory of regeneration now most popular is not correct. There are two theories as to nerve regeneration. The first is that it is central—that is, that the nerve axis cylinders which appear in the distal segment are direct outgrowths from

those in the central segments. This is the older and more popular theory. The "peripheral" theory maintains that the new fibres in the distal segment are formed from pre-existing cells in the distal segment itself. This is the opinion reached by the authors of this book. Their conclusions have an important bearing on the truth or falsity of the neuron theory, because if that theory be true regeneration ought to be impossible in a nerve trunk severed from its trophic centre. Since such regeneration does occur, our authors hold that the neuron theory, in so far at least as it applies to the peripheral nervous system, must be discarded. Whether time will prove that the conclusions of the authors are correct cannot be told; but this much is certain, that fewer men accept the neuron theory now than two years ago. The authors are to be congratulated on their work. There is no padding. The descriptions of the conditions found are brief and clear. The book is well made; the illustrations excellent. C. W. B.

An Experimental and Clinical Research into Certain Problems Relating to Surgical Operations. An Essay Awarded the Alvarenga Prize for 1901 by the College of Physicians of Philadelphia. By George W. Crile, A.M., M.D., Ph.D., Professor of Clinical Surgery, Medical Department, Western Reserve University; Surgeon to St. Alexis' Hospital; Associate Surgeon to Lakeside Hospital, Cleveland. Philadelphia: J. B. Lippincott Co., 1901.

This essay comprises an experimental and clinical research into certain subjects suggested by the writer's practical experience in the operating-room, and includes a study of the effects of severing and mechanically irritating the vagi, the effects of the intravenous infusion of salt solution, the physiological action of cocaine and eucaine, and the effects of temporary closure of the carotid arteries. The experiments were conducted on dogs, cats, and frogs, and extended over a period of three years. The author first reviews the literature of the subject under discussion, then sets down the details of the experiments, and finally points out the practical application of the results of the study, and gives a number of clinical histories to fortify the conclusions reached. The phenomena noted in the laboratory closely corresponded with those met in the operating-room.

Crile finds that no amount of mechanical irritation, even to the extent of destroying the vagi, is sufficient to arrest the heart's action, and that severing one vagus has practically no effect on respiration or circulation. He demonstrates that the blood pressure can be raised little if at all above the normal by the intravenous injection of salt solution, owing to its rapid escape from the vessels and to the automatic action of the medulla. When peripheral resistance is lost, as in fatal shock, no amount of infusion can do more than temporarily restore the blood pressure, and death is inevitable. It is interesting to note that Crile was able to amputate at the shoulder-joint in a woman, seventy-four years of age, without shock or hemorrhage, by employing one-eighth grain of cocaine in solution injected into the brachial plexus. Eleven operations about the head are recorded, in which the annoyance and danger of hemorrhage were entirely obviated by the application of a

specially constructed clamp to the dissected-out carotid artery. Experiments showed that this clamp could be left in position, closing the artery from twenty-four to forty-eight hours, without injury to the vessel's walls.

Unlike many interesting writings on surgical physiology, this volume is distinctly practical, and Dr. Crile deserves a great deal of credit for the infinite pains he has taken in conducting the researches. A sufficient number of illustrations are incorporated to elucidate the text.

F. T. S.

A System of Physiologic Therapeutics. Edited by Solomon Solis Cohen, A.M., M.D. Vol. VI. Dietotherapy and Food in Health. By Nathan S. Davis, Jr., A.M., M.D., Professor of the Principles and Practice of Medicine in Northwestern University Medical School; Physician to Mercer Hospital and Wesley Hospital, Chicago; Member American Medical Association, American Climatological Society, etc. Pp. ix., 372. Philadelphia: P. Blakiston's Son & Co., 1902.

In Part I. the General Principles of Diet and Diet in Health are presented in one hundred and seventy pages, divided into thirteen chapters. Here we find a full presentation of the results of laboratory research, charts and tables based upon them, and special chapters on Diet in Health, Infant Feeding, and Food as a Cause of Disease. Chapter IX. is devoted to beverages, and the alcohol question is conservatively and, indeed, discreetly managed—perhaps with a greater leaning toward discretion than modern investigation would likely carry us. In Part II., Diet in Disease is presented in twelve chapters, opening with one on Feeding of the Sick, which contains many common-sense ideas and practical points. Of these much can be said in praise. Of distinguished mention should be the fact that the author has conscientiously endeavored to translate the results of mathematical research into rules which may guide the practitioner in his labor for the welfare of his patients. In the main we find but little to criticise, and these points are rather matters of individual opinion and personal practice. For a brief, or rather a condensed, statement of what plan should be pursued in the presence of various pathological symptoms and conditions we heartily commend this part to the student and physician. A very complete index adds much to the usefulness of the work. To what may we attribute the successful result of the labors of the author? In the first place, he is writing at an auspicious time. The important investigations of Atwater are accessible, and have reached that point when they have furnished a sound working basis for clinical completion. Next, the analytical studies found in the work of Hutchinson were at hand, for comparison chiefly, at the later period of the work. Finally, the profession is fortunate in possessing an author who combines extensive information and broad, practical experience, with a judicial temperament. The opportunity and the mind to gain the greatest advantage from it have given as a result a compact, practical, and authoritative text-book, without the dogmatism of the laboratory alone or the speculation of unaided experience. The same combination of experiment and observation and theory and practice is bringing about great advances in

other lines of physiological therapeutics—in fact, in therapeutics not within the purview of the editor, yet just so surely physiological—and we take pleasure in noting this volume as one of the best records of the steady progress of the healing art and science which the modern medical spirit and method have given us. The volume is in good company, and yet will stand out with distinction. R. W. W.

CHIRURGIE GASTRO-INTESTINALE. By HENRI HARTMANN, M.D. Editor, GEORGES STEINHEIL. Paris.

THIS book consists of a complete exhibition of the modern surgery of the gastro-intestinal tract. In form it consists of seven lessons or chapters taking up in turn the various surgical procedures of the stomach and intestines, beginning with gastro-enterostomy and ending with excision of the rectum. It also contains an appendix giving a complete list of the author's personal operations in this region of the body. The illustrations are very numerous and particularly pleasing, following the text very closely. For a book of 150 pages it covers the subject wonderfully well. R. G. LE C.

CHARAKA-SAMHITA (translated into English). Published by AVINASH CHANDRA KAVIRATNA, Calcutta. Printed by B. N. Nandi at the Kaviratna Press, 1902.

THIS translation of the ancient Hindu system of medicine is published in fasciculi at short intervals, and is a valuable contribution to medical literature. The translation has been the work of many years, and a debt of gratitude is owing to its editor for issuing it in such an accessible form. It is not only of interest to physicians, but it also presents matter of value to metaphysicians and students of philosophy. F. R. P.

A TEXT-BOOK OF PRACTICAL DIAGNOSIS. The Use of Symptoms in the Diagnosis of Disease. By HOBART AMORY HARE, M.D., Professor of Therapeutics and Materia Medica in the Jefferson Medical College of Philadelphia. Fifth edition, revised and enlarged. Philadelphia and New York: Lea Brothers & Co., 1902.

HARE'S *Diagnosis*, revised and brought up to date, has just appeared in its fifth edition. The fact alone that the work has passed through such numerous editions in a period of six years speaks eloquently in its praise. As in former volumes, various pathological conditions are considered and grouped according to their most salient symptomatological manifestations, and are treated of in the true and practical manner which is characteristic of the author. The text is liberally illustrated by appropriate cuts and half-tones, the sections dealing with the cerebral and spinal nerve tracts being most admirable in this respect. The work will, we have no doubt, as in the past, be one of great practical utility to both student and practitioner as a book of reference and instruction. G. W. N.

INTERNATIONAL CLINICS. Edited by HENRY W. CATTELL, A.M., M.D., Philadelphia, U. S. A., with the assistance of various collaborators. Vol. III. Twelfth series. Pp. 306. Philadelphia: J. B. Lippincott Company, 1902.

THIS volume opens with a remarkably clear and discriminating paper on the Treatment of Typhoid Fever, by Osborne, who presents a well-balanced, common-sense method in which the patient as well as the disease are considered. Mauger supplements this by taking up the question involved in Intestinal Perforation. Crothers, although presenting nothing especially new, gives good advice on the Treatment of Morphinism, and, unlike most men working in narrow specialties, uses proper nomenclature—*i. e.*, morphine, *not* morphia. Hallopeau, writing on the Urticarias, offers a thorough digest of the subject, based on an extended experience, granting that instances of these conditions are as frequent as they were at the St. Louis in our student days under Fournier. In medicine a very substantial article on Splenomyelogenic Leucocythæmia, by Nabarro, a discursive paper by Thayer as to what extent can general practitioners make use of the new diagnostic methods, a further communication on the insect pests of human beings, by Walsh, and three papers of interest both to neurological and general practitioners, by Hopkins, Brower, and Boggen afford much profit and instruction. No complaint can be made by the physician of either the quality or quantity of the material offered. In surgery, Brinton on Some Effects of Firearms at Short Range is likely to add to our knowledge in advancing theories backed by experimental work. Two papers on Dilatation of the Stomach, by Debove and by Cardarelli, cover all aspects of the subject. Willard throws considerable light on the Treatment of Inveterate Club-foot. Obstetrics and Gynecology are represented by two short papers by Baldy and Jardine. An article of unusual importance, and noticeable for its clearness and conciseness, positive, yet not dogmatic, is that of Packard on the Indications for the Removal of the Faucial Tonsils and the Best Methods of Accomplishing It. Syphilis of the Eye, Trachoma, and Acute Mastoiditis are found among other subjects discussed in this section. Pavlof's researches again attract our attention in the paper by one of his pupils—Borrissof—and we are likely to receive both new and novel ideas in the matter of the digestive glands. Schmaus closes the volume with a critical study of the Theory of Inflammation. In variety of topics and number of good names this certainly holds its own with its predecessors; in interest it would be difficult to surpass them. R. W. W.

TRAITÉ DE CHIRURGIE CLINIQUE ET OPERATOIRE. Published by A. LE DENTU et PIERRE DELBET. Volume X., First and Second Parts. Paris: J. B. Baillière et Fils.

THE tenth volume of this well-known system of surgery consists of two parts, the first treating of diseases of the testicle and cord and of the diseases of the female generative organs; the second continues the discussion on gynecological subjects, and also treats of the surgery of the extremities. The two parts number 1330 pages and contain 333 illustrations through the text. They follow in every way the high standard of the volumes that have already appeared. R. G. LE C.

WATER AND WATER SUPPLIES. By JOHN C. THRESH, D.Sc. (London), M.D. (Victoria), D.P.H. (Cambridge); Honorary Diplomate in Public Health, Royal College of Physicians and Surgeons, Ireland; Medical Officer of Health to the Essex County Council; Lecturer on "Public Health," London Hospital Medical College; Fellow of the Institute of Chemistry; Member of the Society of Public Analysts; Associate Member of the British Association of Water-works' Engineers; Examiner in Hygiene, London University, etc. Third edition, revised and enlarged. Pp. 517. Philadelphia: P. Blakiston's Son & Co., 1901.

THE first edition of this most excellent work appeared in 1896, and was a very welcome addition to the literature of a subject which of late years has become one of the most interesting to both lay and professional minds. The second edition improved upon the first, and this, the third, has in its turn improved upon its predecessor, not through the correction of faults and the strengthening of weak points, for such did not exist, but through being kept abreast of the times by the incorporation of the results of constant observation and research. The original chapters have been thoroughly revised, and new chapters dealing with the protection of underground and surface water supplies and with the economics of the subject have been added. In every way the book deserves the highest commendation. C. H.

ORIGINAL RESEARCHES IN THE TREATMENT OF TROPICAL DISEASES WITH INDIGENOUS DRUGS, etc. By HEM CHANDRA SEN, M.D. Cal., Teacher of Materia Medica and Therapeutics, Campbell Medical School; Physician to the Campbell Hospital, Sealdah, Calcutta. Printed at the Record Press, Calcutta, 1902.

A THESIS ON TROPICAL ABSCESS OF THE LIVER. By HEM CHANDRA SEN, M.D. Cal. Printed at the Record Press, Calcutta, 1902.

THESE two pamphlets represent the research and experience of an East Indian physician in the diseases indigenous to his country. The "Original Researches" consists largely of reprints of articles published elsewhere. The author, although of course practising medicine according to modern conceptions, introduces many interesting historical facts drawn from his profound knowledge of Hindoo learning. It is curious in reading these pamphlets to remark how much the ancient Hindoos really anticipated many of our modern ideas of physiology and therapeutics. The author gives a number of extremely interesting formulæ of medicines containing snake venom, derived from the Hindoo systems of therapeutics. He shows a very wide knowledge also of modern medical literature, especially, as would naturally be expected, of the medical literature of England and France.

Dr. Sen is to be congratulated on the interesting work which he has produced. F. R. P.

PROGRESS

OF

MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF

WILLIAM OSLER, M.D.,

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AND

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The Early Diagnosis of Attacks and Relapses of Acute Articular Rheumatism.—ACHALME (*Archives Générales de Médecine*, September, 1902, p. 257) asserts that of all the infectious diseases acute articular rheumatism is the one in which the physician is able to render his patient the greatest service by an early diagnosis. The earlier salicylate medication is used, the more efficacious it is. It shortens the duration and lessens the intensity of the disease, and indirectly by acting in this way diminishes the likelihood of the occurrence of organic heart lesions. He states, therefore, that it would be of the greatest possible importance if a diagnosis of rheumatism could be made in the pre-articular stage.

The writer remarks that, unfortunately, this is rarely possible, owing to the fact that both private and hospital patients seldom come under observation until after there are definite articular symptoms. After referring to the uncertainty and variability of the prodromal symptoms of rheumatism he states that clinical observation has taught him that there is a very important and fairly constant cardiac symptom which precedes the joint manifestations. This symptom is cardiac arrhythmia. This precedes the joint symptoms by four or five days. The pulse is irregular in force and particularly in rhythm. The heart beats occur in groups of two, three, or four. The heart's action is slowed to between 50 and 60. The examination of the heart in initial attacks at this stage usually shows no evidence of valvular disease. The same cardiac arrhythmia also precedes the onset of relapses of articular rheumatism by four or five days. He reports several observations in which the phenomenon was observed in relapse cases in hospital wards. The arrhythmia usually lasts forty-eight or sixty-two hours.

Achalme says that this cardiac irregularity is due either to a disturbance of the nervous mechanism regulating the cardiac action by some toxic substance, or to a lesion of the myocardium resulting from the local infection

with some organism. He believes that the latter hypothesis is the correct one, and advances experimental evidence to support this view. The writer has isolated a bacillus from the blood of several cases of articular rheumatism. He injected into the ear veins of a series of rabbits 2 c.c. of a culture of this organism. In 60 per cent. of the cases a definite cardiac arrhythmia, similar to that observed clinically, occurred. It develops from six to twelve hours after the injection and before any other phenomena. According to the age of the animal death may occur in twenty-four to forty-eight hours, eight days, or recovery may occur. In the young rabbits which die rapidly one finds numerous micro-organisms in clumps in the myocardium. In the older animals which live a little longer one finds a fibrinous pericarditis without organisms in the exudate; the myocardium still shows foci of bacilli, although they are more scattered. If death be delayed for four or five days all the serous cavities contain a serous exudate which is tinged with hæmoglobin, but which is still sterile. Endocarditis did not develop in any of the animals. If the animals recover the temperature falls and the cardiac arrhythmia disappears completely in two or three days.

Achalme believes that his experiments indicate strongly that the cardiac arrhythmia in man is due to a bacterial infection of the myocardium.

Case of Tubercular Tumor of the Spinal Cord in a Child Two Years Old.—Hunter (*Brain, Summer*, 1902, p. 226) reports the case of a child, aged two years, who, at eleven and twenty-two months, was said to have had attacks of "pneumonia." After the last attack the right arm was found paralyzed, and the left subsequently showed some paresis. When the case came under observation there was internal strabismus of the right eye. The head was turned toward the left shoulder. The right arm was completely paralyzed, the muscles being flaccid, but not wasted. There was some paresis and rigidity of the muscles of the left arm. The right leg was paralyzed, but the left not completely so. The knee-jerks were exaggerated and the ankle-clonus was present on both sides. The superficial reflexes were diminished and sensation was everywhere impaired. The child died eventually with unmistakable signs of meningitis.

The autopsy showed tuberculous lesions of both lungs. There was a characteristic tuberculous basilar meningitis. The meninges of the cord were also involved. The cervical enlargement was distinctly more voluminous than normal, and soft in consistency. The enlargement occupied five segments, beginning at the second pair of cervical nerves and ending at the seventh cervical. It was about one and a half inches long. On transverse section the enlargement was found to be due to a tuberculous nodule, occupying the centre of the cord, with but a narrow rim of cord tissue surrounding it. Careful study of fresh and stained sections indicated that the growth had commenced in the right posterior horn, which was almost obliterated. The right anterior horn had been almost entirely destroyed as well. The left anterior and posterior horns were uninvolved throughout. The centre of the nodule had undergone caseation. The stained sections showed that the ganglion cells of the gray matter were well preserved. This fact was probably responsible for the absence of wasting in the par-

alyzed muscles. An ascending degeneration was found in certain of the tracks in the white matter of the cord. This degeneration was attributed to the meningitis rather than to the tumor. The meningitis was believed to have produced its effects through direct action on the ascending fibres themselves, and in part indirectly by its effect on the posterior roots. The writer remarks on the rarity of such tuberculous nodules in the cord, unassociated with tuberculous nodules in other parts of the nervous system.

On a Powerful Specific for the Treatment of Malarial Fever.—GAUTIER (*Archives de Parasitologie*, June, 1902, No. 4, Tome v., p. 569), after a brief historical account of the use of arsenic in the treatment of malaria, states that it was formerly given more for its tonic and alterative effect than as a febrifuge. Moreover, its administration was practically always accompanied by that of quinine.

It is to Gautier that credit is due for demonstrating to the medical profession the beneficial effects of certain organic preparations of arsenic, the so-called cacodylates, in the treatment of malarial cachexia. His discovery of the general therapeutic effects of the cacodylates was made in 1898, in which year he presented a communication before the Academy of Medicine in Paris. With the cacodylates he cured two cases of pernicious malaria, one of which had been suffering from malarial relapses since 1861, and both of which had not yielded satisfactorily to quinine.

Since his first communication he, with the assistance of his medical confrères, some of whom were practising in the French colonies in Africa, has been experimenting with various organic preparations of arsenic in the treatment of malaria. As a result, he finds that disodic methylarsenate, $AsCH_3O_3Na_2$, is a powerful specific in malarial fever. It is closely allied in composition and constitution to sodium dimethylarsenate or cacodylate. The disodic methylarsenate was put on the market in Paris as the "nouveau cacodylate, sel arsenical B, arrhénal." It has been shown to be non-toxic and may be given either by mouth or hypodermically. Gautier recommends its use by subcutaneous injection, as it is more rapid in its effect and causes no local reaction. It is given in doses of from 5 to 10 centigrammes. Gautier has used it in nine cases of pernicious malaria which had not yielded to the administration of quinine. Detailed notes of seven of these cases are given. In some of the cases a single injection of 5 or 10 grains of the disodic methylarsenate caused an immediate cessation of the febrile paroxysms and a complete and persistent disappearance of the malarial organisms. Sometimes two injections, but very rarely more than three, were necessary to produce a permanent cure. The drug has the advantage over quinine in that it does not in any way upset digestion. It seems to stimulate the appetite. It appears to have a remarkable action in rapidly overcoming the malarial anæmia, increases of from 300,000 to over 1,000,000 red cells in forty-eight hours after the first injection being recorded. Gautier believes the drug is a more powerful specific than quinine.

Tabes in Hereditary Syphilitics.—BABINSKI (*La Semaine Médicale*, November 5, 1902, p. 369) says that, although there are not more than twenty recorded cases of tabes in individuals suffering from inherited syphilis, yet

he is inclined to believe that such cases occur more frequently than is generally supposed. He reports two instances which are especially interesting, in that the father of both subjects was himself suffering from locomotor ataxia.

The first patient was a girl, aged twenty-two years, with Hutchinson's teeth. At birth she had anal ulcerations, and attacks of convulsive tic since seven years of age. When seventeen she developed an interstitial keratitis of the type seen in hereditary lues. For the past two years she had been suffering from shooting pains, and her pupils failed to react to light. The girl's father had contracted syphilis and had contaminated his wife at the time she was pregnant. He himself had characteristic signs of tabes; absence of patellar and tendo-Achilles reflexes, vesical symptoms, shooting pains, and Argyll-Robertson pupils.

The second case was a girl, aged fifteen years, whose pupils were inactive to light and whose patellar and tendo-Achilles reflexes were absent. She had vesical symptoms and a left-sided syphilitic choroiditis. The cerebrospinal fluid showed a lymphocytosis. She had mental symptoms resembling either those of dementia præcox or of a diffuse meningo-encephalitis.

Babinski thinks that the knowledge of the occurrence of such cases is of practical importance, in that the thorough and prolonged use of mercury may have a definite influence in retarding the development of the tabetic symptoms.

Treatment by the Tourniquet to Counteract the Vasomotor Spasm of Raynaud's Disease.—CUSHING (*Journal of Nervous and Mental Disease*, November, 1902, p. 657) reports a case in which he adopted the unique treatment of applying a tourniquet for the relief of the pain produced by the vasomotor spasm of Raynaud's disease. The patient, a married woman, aged thirty-five years, was admitted to the Johns Hopkins Hospital under Dr. Osler on October 29, 1901, complaining of "blueness and pains in the extremities." Every winter since childhood she had suffered from attacks of chilblains. During the attacks the toes and fingers would become "red and swollen and would itch and burn." In March, 1901, these symptoms became much aggravated. From that date up to the time of admission a condition of local asphyxia of all the digits had been present, with exacerbations of almost daily occurrence. The arterial spasm was pronounced and was associated with intense pain. On several occasions these attacks were so severe that slight superficial patches of terminal gangrene had affected the pads of one or more of the toes or fingers. Treatment up to admission had been without avail, and there had been almost a daily use of morphine to relieve the pain and induce sleep. After she entered the hospital all the usual methods of treatment, except galvanism, had been tried, without avail.

Raynaud's original theory explaining the local syncope, local cyanosis, thrombosis, and gangrene characterizing the disease known by his name, has not been disproved by subsequent investigators. He believed that the disease was due to an excessive irritability of the vasomotor centre or centres, leading to constriction of the arterioles in certain vascular areas, the exciting cause being a peripheral irritant, usually cold. The treatment naturally must be directed toward overcoming this abnormal vasoconstrictor spasm.

The use of the tourniquet was suggested to Cushing by observing the phenomena following the removal of the tourniquet after operation. After its removal a flushing of the member with arterial blood almost invariably occurs peripherally to the site of constriction. This is presumably due to the temporary paralysis of vasomotor control to the part below the encircling bandage. The constriction causes in some way a "blocking" of the non-medullated fibres. It was the familiarity with the vasodilatation occurring under these circumstances which suggested the employment of a similar procedure as a therapeutic measure to counteract the local conditions of spasm which characterize Raynaud's disease.

The tourniquet was first applied for two minutes on November 10, during an exacerbation of pain and asphyxia in the left upper extremity, a flat rubber bandage being used. It caused some temporary discomfort, but its removal was followed by a much more readily palpable radial artery and great relief to the pain. From this on the tourniquet was applied daily to one or other extremity as conditions indicated. The patient immediately began to make rapid improvement. The pain was always greatly ameliorated, and the attacks became gradually less frequent. Finally they ceased, and she was eventually discharged on December 28, apparently quite well and with the extremities presenting their normal physiological tint.

SURGERY.

UNDER THE CHARGE OF

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The External Dorsal Luxation of the Metacarpophalangeal Joint of the Thumb.—GRISEL (*Revue de Orthopédie*, January, 1902), in a critical and exhaustive review of this subject, states that the pathological anatomy of the complete variety of the dislocation has been well shown by the researches of Vitrac, who gives the following résumé of the lesions: 1. Tearing of the two lateral ligaments. 2. Displacement of the tendon of the long flexor to the outer side of the metacarpal head. 3. Tearing of the phalangeal tendinous sheath, with displacement of the tendon to the outer side of the intersesamoid space. 4. Tearing of the adductor muscle, with or without penetration of this muscle by the head of the sesamoid. The symptoms have been well described in the observations of Guermonprez, and are those of the habitual luxation in the Z position—shortening of the thumb and a variable degree of mobility of the phalanx and three characteristic signs: 1. The situation of the phalanx over the external surface of

the metacarpal. 2. The presence of the flexor tendon, which sometimes may be easily shown, over the external surface of the metacarpal. 3. The forced adduction of the metacarpal bone with its head prominent under the skin of the inferior portion and internal to the thenar eminence in the region of the metacarpal bone of the index finger. This permanent adduction is a double obstacle to reduction because: 1. The adduction being complete it is impossible to carry the bone further away so as to relax the muscular buttonhole at the moment of reduction. 2. The metacarpal bone falls down into the palm of the hand and increases the difficulty of releasing the articular head of the phalanx.

In the complete external dorsal luxation the symptoms are: 1. The situation of the phalanx over the external surface of the metacarpal bone. 2. The presence of the tendon to the outer side of the head of the metacarpal bone. 3. Forced adduction of the metacarpal bone. Beyond the phalanx to the outer side of the metacarpal one may see: 1. The lateral ligaments in part torn and in part detached and having carried away with them the periosteum and lateral portion of the metacarpal bone. 2. The dorsal portion of the capsule and the periosteum of the dorsal surface are elevated by the passing of the phalanx over the back of the metacarpal bone. 3. The turning back of the gleno-sesamoid band which remains adherent to the phalanx. 4. The existence of a buttonhole through which passes the metacarpal bone; the internal edge of which is formed by the adductor, and the external edge by the flexor tendon, external sesamoid bone, and external sesamoid muscle, and the eyelet corresponds to the internal sesamoid. 5. The flexor tendon is maintained between the sesamoids in the fibrous tissue which crosses obliquely the external border of the metacarpal bone to reach the slip of the short flexor.

The causes of the irreducibility of the external complex luxation are: 1. The flexor tendon being torn from its phalangeal sheath is no longer next the phalanx and the sesamoid during the manœuvres of reduction. It either remains curled up near the metacarpal bone, or it is interposed between the articular surfaces. 2. The sesamoid bones may not constitute an obstacle to reduction if there is a sufficient separation of the phalanx and the metacarpal bones for them to pass. 3. A luxation that is irreducible, notwithstanding the separation of the two bones sufficient for the passage of the sesamoids, may be reduced by section of the flexor tendon.

In those cases of habitual complicated luxation which often present themselves for treatment, where the section of the glenoid ligament is not sufficient, the surgeon has the choice of any one of three solutions of the problem: 1. The complete elevation of the gleno-sesamoid covering. 2. Section of the lateral ligaments and the attachments of the sesamoid muscles. 3. Resection of the head of the metacarpal bone.

Femoral Osteotomy and Ostectomy in Ankylosis of the Hip in Malposition and in Certain Fractures of the Femur United in Malposition.—VINCENT (*Revue de Chir.*, 1902, No. 10), after a detailed review of the subject, states in conclusion: 1. The application of the vise of Lorenz during the course of osteotomy for the relief of viciously consolidated fracture of the diaphysis of the femur, with marked over-riding of the fragments, is a

useful procedure. It is much more powerful than manual traction, and may be used with sureness and precision. 2. This method is especially valuable in the bony section in the form of a Z, which gives to the reduced osseous surfaces a true notch, and permits of the advantages of the oblique osteotomy for the coaptation of the fragments and avoids the necessity of applying continuous extension, which is painful and uncertain in its results.

The Fracture of Dupuytren.—Mally and Richon (*Revue de Chir.*, 1902, No. 10), after an exhaustive review of the subject, state in conclusion: 1. By the term fracture of Dupuytren is meant the bimalleolar fracture of the leg by adduction, that is to say, fracture by tearing away of the internal malleolus from its base or its end, or, more rarely, laceration of the internal lateral ligament, fracture of the fibula to the upper side of the inferior tibiofibular ligament, and separation of the ends of the bones forming the inferior tibiofibular articulation; this last may not occur. It is always an articular fracture. 2. The prognosis is extremely grave from the point of view of function. In spite of well-directed therapeutics, at the moment when the consolidation should be theoretically well advanced one may observe, during the period of convalescence, two sorts of secondary complications: *a*. First and almost constant, but of variable severity, is the muscular atrophy of muscular origin affecting unequally the motor muscles of the tibiotarsal articulation, and at the same time one sees the various cutaneous and vasomotor trophic disturbances. *b*. A secondary deviation of the foot progressive to valgus. 3. This muscular atrophy has the characteristics of the reflex muscular atrophy, and permits in consequence the atrophy of a certain number of the motor cells of the anterior horns of the cord in the region of the dorsolumbar enlargement. 4. The existence of trophic phenomena in the skin and vasomotor system with the muscular atrophy permits the belief that the deviation of the foot has as its primary cause a similar trophic trouble, which causes alteration of the structure of the ligaments and interference with the normal progress of ossification of the callus. These primary alterations of the ligaments and the callus are, according to the authors, of trophic origin, and allow the weight of the body to efface the plantar arch, permitting the astragalus to "see-saw" downward and inward. This movement of the astragalus is assisted by the stretching of the internal ligament by the callus, and the forcing to the outer side of the fibular malleolus, which transmits a portion of the weight of the body upward and outward to the external face of the astragalus, the fibular callus yields and the bone becomes ultimately bent. 5. The spinal lesions which cause the trophic phenomena have not been exactly determined; those which cause the atrophy of the muscles consist essentially in the diminution of the motor cells of the anterior horn with atrophy of their pigment and effacement of their cylindrical prolongations. 6. The pathogeny that the authors have proposed to explain these secondary complications is entirely new and is justified by the statement of Tillaux: "There is no other fracture in which the treatment is more important and more difficult than in the bimalleolar fracture by abduction." 7. The immediate treatment should consist in the application of a dressing which will accurately maintain reduction; the dressing should be so applied that the internal

malleolar region is freely accessible. In order to fulfil these indications the authors have proposed the use of a plaster-of-Paris trough of special design, the foot first being placed in forced adduction. If the œdema of the soft parts is very pronounced, massage and evaporating lotions should be used for several days preceding attempts at reduction. If the fracture is compound, reduction should be preceded by a vigorous disinfection of the wound. 8. The callus almost always is retarded in its consolidation, and so when one removes the plaster trough it is essential to maintain the instep not only laterally but also underneath the arch by a suitable bandage, so as to prevent the secondary deviation to the position of valgus. 9. The muscular atrophy which is peculiar to these articular fractures, and which is spasmodic, demands for its relief an altogether different treatment from that of simple atrophy. All forcible manipulations of the joint and the direct excitation of the muscles by either massage or electricity are absolutely contraindicated. Local sedative applications, with counterirritation over the spine, may prove to be of value. The author's experience shows that static electricity best fulfils this last indication. 10. Union in bad position is a serious condition, and demands surgical intervention for its relief. According to the severity of the case, one may have recourse to either simple or wedge-shaped osteotomy, resection, astragalectomy, and, finally, the wiring together of those fragments which show no tendency to become united.

THERAPEUTICS.

UNDER THE CHARGE OF

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Concerning a New Series of Synthetic Salts of the Nucleids of Iron, Copper, Mercury, and Silver.—DR. E. R. LARNED gives a summary of the steps which have led up to the commercial production of these new compounds of nucleinic acid and the metals—iron, copper, mercury, and silver. They are known under the trade names of *ferrinol*, *cuprol*, *mercurol*, and *argol*, respectively. He summarizes their advantages as follows: 1. These new salts of nucleinic acid are rational reconstructives; they are true tonics; they increase physiological resistance; they increase the functional activity of secretory organs. 2. They are powerful germicides, and are not harmful to the tissues. 3. If the present state of our knowledge of the nucleins and leucocytosis is correct, then the nucleid is the proper form for the administration of the metals.—*Therapeutic Gazette*, 1902, vol. xxvi. p. 593.

Peridynamin.—Dr. O. Liebreich writes on a new iron preparation by this name. In its action it resembles ferratin, and is useful as a hæmoglobin former.—*Therapeutische Monatshefte*, 1902, vol. xvi. p. 423.

The Serum of Trunecek in Arterio-sclerosis.—Dr. S. Sehouriguine recalls the serum that Trunecek devised over a year ago for the treatment of arterio-sclerosis. This was: sodium sulphate, 16; sodium chloride, 140; sodium phosphate, 5; sodium carbonate, 7; potassium sulphate, 13; water 1440. The author reports his results obtained with a patient, aged eighty years, suffering from arterio-sclerosis. The symptoms were marked depression and pain over the heart region. During a space of five weeks seven injections were given. The oppression diminished, cyanosis of the lips disappeared, and the old man declared himself young again.—*Thérapeutique moderne Russe*, 1902, vol. v. p. 20.

Agurin: A New Diuretic.—Dr. M. Salacoln has administered to a certain number of patients a new diuretic obtained from theobromine, and called agurin (a double salt of sodium acetate and theobromine). In all of his cases he found a constant increase in the amount of urine passed, with a maximal amount occurring three to five days after the administration of the drug. There was also a slight increase in the arterial pressure. In arterio-sclerosis with cardiac or renal disease the diuresis has been more marked and the beneficial effects more pronounced than in cases of hepatic cirrhosis. The remedy was well borne, and could be employed for several weeks without discomfort. In one case of marked arterio-sclerosis there was gastric irritability. The dose is 7 grains at hour intervals. It can also be given by the rectum.—*Thèse de Paris*, 1902, No. 566.

The Therapeutic Value of the Alkaline Vichy Waters.—Dr. Oscar Liebreich speaks of the differences of natural and artificial mineral waters, claiming that no amount of detailed chemical analysis and subsequent compounding can ever duplicate the natural mineral waters. This is due to several factors—inaccuracies of weighing, the presence of bodies which split up and are destroyed in chemical manipulation; and then, again, from the standpoint of manufacturing, the impossibility of obtaining pure products at reasonable prices. Further, nearly all natural mineral waters contain a colloid substance, formerly termed glairin; this has never been reproduced, and in Leibreich's opinion it is of importance therapeutically. In natural waters, also, carbon dioxide exists in two forms—the anhydride and the hydrate. Artificial waters are impregnated only with the anhydride. Of the different Vichy springs, he points out that they are not identical in character, but, broadly speaking, they are very similar with regard to their alkalinity. Nevertheless, the two springs which are mostly used—the Grande Grille and the Célestins—have different therapeutical effects. The modern therapeutist is bound to take into account the chemical composition of the remedies used, and an ingredient, even when present in very small quantities, is capable of bringing about some action, especially since the presence of other ingredients may cause synergistic action. Of the various diseased or disordered states that are best adapted to treatment by these

mineral waters the author speaks of gout and diabetes mellitus—especially of pancreatic origin—and particularly for the prevention of diabetic coma. In chronic catarrhal diseases of the stomach the alkaline mineral waters have been regarded almost as specifics. They increase peristalsis, diminish the hyperacidity of the mucous glands, and stimulate the production of the digestive ferments. In gastric ulceration in anæmia it is desirable to keep the secretions alkaline by these waters. In Reichmann's disease they are indicated. The Vichy waters are also available in diseases of the liver, particularly in those conditions that favor the formation of gallstones. Other conditions are mentioned by the author, such as albuminuria and certain skin diseases.—*British Medical Journal*, 1902, No. 2180, p. 1159.

Physical Therapy.—Dr. Franz C. Müller, of Munich gives a complete review of the newer literature on balneotherapy, hydrotherapy, and light therapy.—*Schmidt's Jahrbücher*, 1902, vol. cclxxvi. p. 6.

Dangers of Subcutaneous Gelatin Injections.—Drs. Margoniner and Hirsch point out that for a long time pain and a feeling of tension, abscess formation, and fever were considered the only untoward symptoms following the injection of glycerin, until several cases of tetanus were reported, which necessitates extreme care in proper sterilization. The author dissolves 2 grammes in 100 cubic centimetres of warm physiological salt solution and then exposes the flask for one hour to live steam at 100° C. The injection must be made by means of a syringe which permits of perfect sterilization. The results were very satisfactory, and gelatin was found to be an excellent hæmostatic especially in prolonged cases of hæmoptysis. The emboli which occasionally have been reported are not the result of the gelatin, but may follow any subcutaneous injection.—*Therapeutische Monatshefte*, 1902, Heft vii. S. 334.

X-ray Treatment of Carcinoma.—Drs. Wallace Johnson and Walter H. Merrill publish a table showing that of 16 cases of epithelioma treated, regardless of their length of existence, extent of tissue involved, and previous treatment, 10 patients, or 62.5 per cent., are apparently cured; and, in addition, 4 cases, or 25 per cent., show improvement, and 3 of these give promise of ultimate recovery under further treatment. Only 2 cases, or 12.5 per cent., failed to derive benefit from the treatment other than alleviation of pain and diminution of discharge. Of 7 carcinomas treated, all of which were classified as inoperable by the surgeons, none showed any improvement beyond relief from pain and probably a temporary delay in the final fatal termination. Lupus vulgaris can be cured, fibromas show no change at all. Three or four semiweekly exposures of four to five minutes' duration were sufficient to produce a reaction.—*American Medicine*, 1902, vol. iv. p. 217.

Drops as Dose Measures.—Dr. M. I. Wilbert publishes several tables which show that little or no uniformity can be expected in comparative results on the number of drops to be obtained from different dropping surfaces. The irregularities are so apparent and so great that they suggest that every dropping surface is a law unto itself with each and every liquid. A reasonable

and practical standard would be to accept a drop of water as being equivalent to the tenth part of a gramme. This would be a convenient number to remember and would be in harmony with the metric system, and, in addition to this, it would represent the most readily obtained drop of water, dropping in seconds from the greatest variety of dropping surfaces. Then, too, all possible error would be on the side of safety. From the writer's experience it would appear that the difference in the space and thickness of the lip of a vial is a greater factor in the size of the resulting drop than the quantity of liquid it contains, and a rough or ground-glass surface offers more attraction for the spread of a liquid and would give a larger and more uniform drop of water than one that is quite smooth. A clean, smooth surface, however, would give more uniform and larger drops than one coated with even the slightest trace of fat or oil. Of course, it would be most simple to do away with drops entirely, but for potent remedies which are constantly increased or decreased in dose they are indispensable.—*American Journal of Pharmacy*, 1902, No. 8, p. 375.

Relation Between the Chemistry and the Physiological Action of Morphine.—Dr. E. Vahlen, assuming from the large size of the morphine molecule that not all of its atoms take part in its physiological action, has attempted to isolate that physiologically interesting nucleus upon which most of the efficacy depends. In so comparatively new a branch of pharmacology the difficulties of research are obvious, since it is only rarely that by the breaking up of a molecule components are obtained which resemble the mother-substance in effect. More often one common ingredient is found in a number of drugs of the same action and close chemical relation, as in the case of the purin obtained from caffeine, theobromine, and allied alkaloids, upon which most of their action depends. In starting his experiments the author assumed that the phenanthrene nucleus was the chief carrier of its function; and as it seemed desirable to add nitrogen—an important element in most alkaloids—he discovered a synthetic combination of the two, which he named morphigenin. Chemically, it is oxyamidophenanthrene, and it seems, indeed, as if it closely resembles morphine physiologically—so much so that a readily soluble derivative has been brought on the market under the name of epiosin. There are other products with the same nucleus, and also narcotic in effect, that could be formed, as by the action of zinc chloride giving morphigenin chloride. Several could be obtained by combining sulpho-acids with morphigenin, but no stable compounds resulted from all these experiments, and so their importance is diminished. To manufacture epiosin, one part of morphigenin chloride, with three parts of sodium acetate, twelve parts of absolute alcohol, and one and one-half parts of an aqueous methylamine solution, 33 per cent. in strength, are heated for two hours in the water-bath, with subsequent evaporation and extraction with chloroform. Epiosin, chemically, is a methyldiphenylenimidazol. It melts at 383° F., and is readily soluble in alcohol and chlorform, and its chlorides are soluble in water. When it is injected into frogs the functions of the cerebrum are first paralyzed, and later those of the spinal cord; when injected into dogs, there is a blunting of the sense of pain, not leading to sleep, a sluggish corneal reflex, involun-

tary defecation, urination, and salivation, and a slight rise of blood pressure, with slowed and shallow breathing. The pupillary changes were, unfortunately, not recorded, but no marked myosis occurred. Convulsive twitchings were observed when larger doses were used. On man it showed a ready relief of pain, with sleep and no after-effects. The dose of epiosin chloride is one-seventh to 2 grains, and 4 grains correspond to 1 grain of dionin.—*Archiv für Experimental Pathologie und Pharmacologie*, 1902, Band xlvii. p. 368.

Decomposition of Iodides in the Body.—Dr. A. Stepanow analyzed the different organs for nitrites with sulphanilic acid, naphthylamin, and acetic acid, in order to explain the splitting up of potassium iodide in the body. They were found present in the white substance of the brain, lungs, bronchi, parotid, duodenum, medulla of kidney, suprarenals, testicles, and in the parotids, while in the gray brain-matter, liver, stomach, spleen, cortex of kidney, and blood they could not be detected. The conclusion is drawn that in decomposing the iodides, the nitrites, in conjunction with the carbon dioxide of the tissues, play an important part, but that there are also other factors which are not known.—*Archiv für Experimental Pathologie und Pharmakologie*, 1902, Band xlvii. p. 411.

Some Principles of the Brain of the Horse.—Dr. A. Bethe was able by the following method to isolate several new principles occurring in the central nervous system of the horse. The brain and spinal cord of recently slaughtered animals were freed as much as possible from membranes and large vessels, comminuted, and triturated with water containing much copper chloride until a distinct green color remained after several days. Potash lye up to a distinct violet color was then added, and, on the following day, alcohol and hydrochloric acid, which removed biuret, cholesterin, and certain bodies containing phosphorus, which can easily be isolated. The residue was again treated with potash lye, acidified with acetic acid, and dehydrated with alcohol. On dissolving in chloroform, concentrating, and dropping into ethylic ether, a fine green precipitate resulted, while the ether itself took on a dark green color. The precipitate was found to consist of three definite substances: (*a*) *Amidocerebrininic acid-glycoside*, easily soluble in benzol, chloroform, and hot alcohol, insoluble in ethylic and petroleum ether. On boiling with water it also dissolved in this, yielding an opalescent, gelatinous solution. Precipitation occurred with barium in hot alcoholic and with copper in slightly alkaline or acid solutions. The melting point was found to be 354° F., and analysis gave the following figures: C = 70.19, H = 11.08, N = 1.86. By boiling with hydrochloric acid, sugar (galactose), an acid free from nitrogen (cerebrininic acid), and a nitrogenous principle (cerebrininic acid amide) resulted. (*b*) *Phrenin*, soluble in hot alcohol, insoluble in ether, and precipitating well with barium, but not with copper. The melting point could not be definitely determined, but seemed to lie somewhere between 190° and 213° F. The elementary analysis gave C = 71.9, H = 11.95, N = 1.45, and it seemed as if the substance represented an amido-acid, or an acid amide with a free acid molecule. (*c*) *Cerebrinin-phosphoric acid*, a neutral, crystalline body, soluble

in hot alcohol and ether and in chloroform, and melting at 321° to 323° F. By boiling with hydrochloric acid it split up into five distinct substances: (1) Galactose, (2) phosphoric acid, (3) cerebrininic acid, (4) amido-cerebrininic acid, and (5) a nitrogenous water-soluble principle.— *Archiv fur Experimental Pathologie und Pharmakologie*, 1902, Band xlviii. p. 73.

PEDIATRICS.

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The Leucocyte Count in the Diagnosis of Diseases of Children.—George Douglas Head (*Archives of Pediatrics*, April, 1902, p. 253) calls attention to the value of leucocyte counts in the differential diagnosis of certain diseases of early life. From the conclusions of various observers it is probable that in healthy infants a mild degree of leucocytosis occurs during the first year of life, and this is somewhat diminished during the second year; but beyond the age of two years in healthy children the count is not different from that of adults. From one to two years the count may be of considerable value if one is careful to exclude the leucocytosis of digestion; but even at this age the chief value of the procedure must be to assist in the identification of such diseases as are characterized by a diminution rather than an increase in the leucocytes. This group of diseases includes typhoid fever, influenza, measles, malarial fever, and miliary tuberculosis, and, perhaps, tuberculous meningitis. Beyond two years of age the leucocyte count in diseases of children is as invariable and as fixed as in diseases of adult life.

In typhoid fever in children the low leucocyte count is constant, being raised above the normal figure only in the presence of complications. If in a case of suspected typhoid fever in a child the count is over 10,000, the diagnosis of uncomplicated typhoid fever cannot be entertained, and a complication is to be looked for whether the symptoms indicate it or not. But the count is of most value when the clinical symptoms have narrowed the diagnosis to a choice between typhoid fever, on the one hand, and meningitis, osteomyelitis, appendicitis, or some other infection; for in all the latter group there is an increase of the white blood count.

In adults typhoid hemorrhage or perforation is followed by a prompt rise in the number of leucocytes. There are, however, numerous exceptions to the rule, and practically the knowledge furnished by the white count is this: if, in a case of typhoid fever, symptoms pointing to perforation or hemorrhage are observed, a rise in the leucocytes strengthens the evidence that perforation or hemorrhage exists. While none of the cases in the series of children's

cases collected by the author was thus complicated, it is to be presumed that the rule in adult cases would be followed.

Appendicitis in children, as in adults, is accompanied by a well-marked leucocytosis. The count is thus of value in differentiating appendicitis from attacks of abdominal pain from renal calculus, gallstones, acute intestinal obstruction, and typhoid fever, all of which have a normal or diminished count. From acute gastritis, acute nephritis, or acute enterocolitis, all of which cause leucocytosis, differentiation could not be made. Again, when the symptoms of appendicitis give no clue to the course the disease is pursuing the leucocyte count is often of valuable assistance in following the course of the inflammation. No conclusions, however, can be drawn concerning the severity of a given case, unless successive counts have been made from the outset of the disease.

In lobar pneumonia a pronounced leucocytosis is encountered. An average of the cases under five years gives 41,090, while for cases over five years the average count is 26,800. The number of complicated cases is too small to give satisfactory conclusions.

In cases of pneumonia simulating typhoid, malaria, or influenza, a high leucocytosis rules out these three common infections, but is of no value in distinguishing it from cerebro-spinal meningitis or appendicitis.

Only three cases of bronchopneumonia are included in the series, but from these it is probable that while leucocytosis accompanies the disease it is not as pronounced as pneumonia.

Meningitis (five cases) shows a pronounced leucocytosis, ranging from 14,200 to 40,600, which appears early in the disease and continues till death. Complications do not modify it. In the diagnosis between meningitis and uncomplicated typhoid fever the count, as already indicated, is almost, if not absolutely, diagnostic. Between meningitis and hysteria the count in two cases seen by the author has been diagnostic (6300 and 9000). As between meningitis and brain tumors, one case of the latter disease examined by the writer gave a count of 5500 in the second week of severe symptoms.

In diagnosis between tuberculous and non-tuberculous forms of meningitis no cases of children have been reported, and the counts in adults are conflicting.

In influenza in children it is probable that a normal or reduced count occurs in the uncomplicated cases, as in adults. The test will, therefore, be of value in differentiation from meningitis, and also in establishing the presence of a complication like lobar pneumonia.

In diphtheria the count is of little practical value. In measles, however, the count is normal or below during the whole course of the disease, but complications, such as bronchopneumonia, severe bronchitis, or otitis media, cause a leucocytosis in some cases.

German measles, according to Cabot, shows no leucocytosis, and mild scarlatina, according to Turk, shows nearly a normal number of leucocytes. If the infection is severe and the diagnosis lies between scarlatina and measles, leucocytosis would point to the former, a normal count to the latter.

In scarlet fever leucocytosis begins a day or so before the rash appears, reaches its height about the time of the full development of the exanthem, and falls with the fading of the rash, or may persist some days longer.

In variola, as already proven by Rick, no leucocytosis occurs prior to the formation of the vesicles; with their appearance the count rises, and reaches its height as the exudate becomes purulent. In very mild cases no increase occurs during the course of the disease. These statements probably apply to children, as well as adults. Since the initial rash of variola sometimes resembles that of scarlet fever, the white count might give valuable information early in the disease.

OBSTETRICS.

UNDER THE CHARGE OF

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Diagnosis by Vaginal Examination.—In the *Journal of Obstetrics of the British Empire*, November, 1902, STEPHENSON contributes an excellent paper upon this subject. He calls attention to the fact that with proper care, vaginal examinations are attended with but little danger, and that important knowledge regarding parturition can be obtained by this procedure only.

Although the usual belief is that the occiput is seldom upon the right side and anterior, or upon the left side and posterior, Stephenson finds this is erroneous. More frequently than ordinary statistics would lead us to believe, he has found the occiput anterior and upon the right or posterior and upon the left.

He also calls attention to the fact that in a pelvis of average dimensions and with a pelvic floor and perineum uninjured and not relaxed, it is impossible to touch the promontory of the sacrum. Many books and articles upon the subject of vaginal examination assert that the sacrum can readily be palpated including the promontory, an assertion which experience does not prove. If the observer finds that upon vaginal examination his fingers come readily in contact with the promontory of the sacrum he must conclude that the pelvis is considerably contracted.

In order to accurately appreciate what is meant by vaginal examination, Stephenson urges that the sort of vaginal examination made should be definitely stated, whether it is the ordinary examination or whether it be an examination made under partial anæsthesia or with pressure especially adapted to reach the higher points of the posterior pelvic wall. He refers in his paper to what is termed "ordinary vaginal examination."

Again, he calls attention to the fact that a frequent error is made in stating that upon vaginal examination as ordinarily made both fontanelles can be reached. This is never the case, but, on the contrary but one fontanelle

and the sagittal suture are available by ordinary vaginal examination. The same is true regarding the detection of the ear of the child, for upon ordinary examination, this cannot be felt.

Stephenson defines the normal range of vaginal examination as corresponding with the ligamentous boundary of the pelvic outlet. He asserts that in the upper part of a normal pelvis the fingers command only the anterior half of the pelvis, while in the lower division and on the pelvic floor they reach slightly beyond the transverse plane. He proves these statements by measuring the length of the fingers, finding that when two fingers are inserted the nearest distance at which effective touch can be made is three and one-half inches. He believes that in ordinary examinations the dorsal surface of the two flexed fingers does not pass beyond the transverse line joining the anterior margin of the tuberosities of the ischia. Even with strong pressure they cannot be forced beyond the plane of the outlet. He believes that when the fingers are fully introduced in the mesial line the tactile portion corresponds fairly with the central line of the pelvis. The os is usually found central, but is at times displaced. When the os is moderately dilated the fontanelles are not accessible, but the sagittal suture can be felt crossing the os. When the os is more dilated, or if the fingers can be passed within, a fontanelle may be felt. If it is the smaller the head is flexed; if the larger the head is somewhat extended. In estimating the degree of flexion, attention must be given to the presence or absence by palpation of the larger fontanelle. The more readily this is felt the greater the degree of extension which is present. He also calls attention to the fact that when all of the anterior fontanelle is not accessible a portion of it resembles normally the posterior fontanelle in being a small space enclosed by three bony lines.

Rapid Dilatation of the Uterus by Bossi's Dilator.—Before the Edinburgh Obstetrical Society at its meeting on November 12, 1902, SIMPSON (*British Medical Journal*, November 29, 1902) reported the case of a young primipara admitted to the Royal Maternity Hospital in violent eclampsia. The urine was highly albuminous and the cervix barely admitted one finger. In addition to treatment addressed to elimination and the control of the nervous system, under chloroform the cervix was gradually dilated with Bossi's dilator, securing complete opening of the cervix in twenty minutes. The child was delivered by axis traction forceps, but did not live. The patient had a number of convulsions afterward, in all eighteen during her treatment. She made a tedious but complete recovery.

At the same meeting FROST reported the case of a patient aged forty, eight months pregnant, seized with eclampsia. As the patient was profoundly unconscious, it was thought necessary to empty the uterus as soon as possible. Bossi's dilator was employed and the patient delivered by forceps. As the cervix was scarcely opened it was necessary to introduce the dilator without the shield. When the index registered 3½ cm. of dilatation the shields were applied, and the procedure continued until 9½ cm. of dilatation had been effected, when the instrument was finally withdrawn. The operation up to this point occupied thirty-five minutes. The application of the forceps was difficult, as the head lay above the brim and was movable. Convulsions con-

tinued for seventeen hours after delivery, growing gradually less violent. The patient regained consciousness about forty hours after delivery. No sedatives were employed, but hot packs were used persistently to secure thorough sweating. The albumin in the urine gradually decreased and the urea gradually increased. The patient was markedly jaundiced during convalescence, but finally made a satisfactory recovery. The child also survived.

In the *Centralblatt für Gynäkologie*, 1902, No 47, KNAPP adds a further paper to his original communication in the *Wiener Wochenschrift*, 1902, Nos. 41 and 42. He describes Bossi's dilator with illustrations, and continues to endorse it.

From the clinic in Carlsruhe comes a report by WAGNER (*Centralblatt für Gynäkologie*, 1902, No. 47) of three cases in which Bossi's dilator was used to open the cervix.

The first of these was a multipara who had had colpotomy performed previously to her present labor. The cervix was very slow in dilating, and the patient weak and highly nervous. Bossi's dilator was introduced after narcosis, and gave the patient but little suffering. In thirty minutes the cervix was completely dilated, and the patient shortly afterward could be delivered with Tarnier's forceps. Mother and child recovered well.

His second case was that of a multipara, aged forty-five, with slightly contracted pelvis, who had had very large children in transverse presentation. All the children had perished soon after labor. With the past history it was thought best to induce labor before the child became excessively large. The child was in the second transverse position, the back anterior. During dilatation the patient had almost no pains, and in sixty minutes the cervix was completely opened without rupturing the membranes. When dilatation had been complete for five minutes the membranes were ruptured, version made, and the child delivered. Considerable difficulty was experienced, as the arms were above the head, and the child was born asphyxiated and could not be made to breathe. As there was free hemorrhage, examination revealed laceration of the cervix, with arterial bleeding. This was closed by suture, and the patient made a good recovery. It is thought that the large head of the child tore the cervix and not the instrument used for dilatation.

The third case was that of a multipara, aged twenty-five, pregnant five months, who had suffered with profuse hemorrhage for three weeks. As the finger could not be introduced through the cervix to make accurate diagnosis, Bossi's dilator was used and a thorough examination made, finding a placenta prævia. The cervix and vagina were thoroughly tamponed, and the patient had sharp rise of temperature. On the following day the dilator was again employed, the membranes ruptured, and a macerated child delivered by version and extraction. The placenta had been deeply detached from the anterior wall of the uterus. In each of these cases the instrument worked to great satisfaction.

BISCHOFF, from the clinic at Bonn (*Centralblatt für Gynäkologie*, 1902, No. 47), reports five cases in which Bossi's dilator was employed with satisfaction. Three were cases of eclampsia and two of contracted pelvis. One of the eclamptic cases had contracted pelvis also. The children were delivered by craniotomy, version, and the use of forceps in accordance with the needs of each case. It was found that laceration of the cervix followed the use of

the instrument, but not to a severe degree and not sufficiently to bring the patient into danger. Bischoff believes that when the case is not serious and haste is not imperative the cervix can be dilated with less damage by other methods, such as the use of the bougie and elastic bags. Where, however, cases are brought into the hospital for operation, requiring delivery, where antiseptic precautions can be carried out and any operation necessary done promptly, the instrument should have a place and should be employed.

To the foregoing cases LANGHOFF (*Centralblatt für Gynäkologie*, 1902, No. 47) adds a case of eclampsia in which Bossi's dilator was used with excellent result.

MUELLER, of Munich, and FROMMER describe metal dilators similar in action to Bossi's, and urge the value of their use in properly selected cases.

Complete Inversion of the Uterus of Seven Months' Duration.—TAYLOR (*Journal of Obstetrics of the British Empire*, November, 1902) reports a case of a primipara in labor two days before delivery, who suffered severely from hemorrhage after the birth of the child. The condition was not recognized, and seven months after the occurrence of uterine inversion the patient was seen and a correct diagnosis made. Other means failing to reduce the inversion, the patient was stimulated for a short time, and under aseptic precautions, an anæsthetic having been given, the anterior vaginal wall was opened by a transverse incision as close to the inversion as possible. The uterus had been inverted so long that it had detached itself from its usual union with the bladder. The peritoneum was pushed up and the anterior margin of the cervix seized on each side by volsella forceps and the uterus opened between them with straight scissors. The appendages were almost entirely buried within the cup of the inversion. As the appendages were adherent it was necessary to carry the division in the uterus up to the fundus before they could be separated and the inversion thoroughly reduced. When this had been accomplished it was found that the peritoneal surface of the uterus was much smaller than the mucous surface, and here Taylor thinks that the uterine wall should have been resected to make a perfect closure. As the patient's condition was critical this was not done, but the uterus was closed with fine silk. An iodoform gauze drain was left between the uterus and the bladder. The patient made a tedious recovery, and the silk suture placed in the uterus had to be removed. She finally became completely convalescent, and on careful examination no trace of the inversion could be found.

The Operative Treatment of Face Presentation with Posterior Turning of the Chin.—STROGANOFF presented at a meeting of the Russian Society for Obstetrics and Gynecology (*Monatsschrift für Geburtshülfe und Gynäkologie*, Band xvi., Heft 5, 1902) a paper upon this subject in which he described some of the results which he had obtained in these cases.

The first was a multipara with fairly sized pelvis in whom the fœtus presented with the chin directed toward the right side and behind. The patient was seized with eclampsia. The head descended very slowly, a swelling forming upon the forehead and both cheeks. The long diameter of the face was in an oblique diameter of the pelvis. Simpson's forceps was applied in the

left oblique diameter of the pelvis, and the chin raised as much as possible until the long diameter of the face was in the transverse diameter of the pelvis. The forceps was then removed and reapplied in the right oblique diameter. The chin slowly rotated to the front, but scarcely sufficiently for delivery. Simpson's forceps was then laid aside, and those of Lazariewitsch applied in the right oblique diameter, bringing the chin to the front and resulting in the birth of the child. Slight swelling was seen on the forehead and cheeks of the child. The posterior vaginal wall was injured, and also the left labium. The patient was discharged in good condition on the twelfth day. The child died six hours after birth.

The second case was that of a primipara with brow presentation, the small fontanelle upon the left side near the junction of the ilium and pubes and the head in the pelvis. The lower uterine segment became greatly distended the patient's pulse became rapid, and exhaustion threatened. It was determined to try Lange's method of applying the forceps in the same oblique diameter occupied by the head. Simpson's forceps was applied without difficulty. Traction was made very slowly, the head rotating to the front, and delivery occurring with the usual mechanism of face presentation. When the chin was brought under the pubes the forceps was removed and the head brought out by manipulation. The child was asphyxiated, but soon revived. There was a large scalp tumor from pressure and paralysis of the facial nerve. The mother had slight laceration of the perineum. Mother and child made a good recovery.

Case third was also a primipara having a flattened pelvis, the chin of the child directed to the right side and posteriorly. The mother's heart action increased in rapidity, her temperature rose somewhat, and the heart sounds of the child were not so good. As the cervix was partially dilated, an effort was made to perform version, but this failed, and, the cervix dilating no further, the forceps was applied. The head then stood between the transverse and right oblique diameter in the entrance of the pelvis, the chin on the right side and posterior, the forehead on the left and anterior. The forceps was applied after Lange's method in the same oblique diameter with the head, and extraction made without special difficulty. The chin rotated to the front. The cord was wrapped three times about the neck of the child, and the child was born deeply asphyxiated, and could not be revived. The mother had a mild endometritis during the puerperal period, but was discharged convalescent on the eighth day. She had considerable laceration of the cervix.

Stroganoff believes that when the mother's condition demands prompt delivery efforts should be made in these cases to bring down the head and cause anterior rotation by the use of forceps. He recognizes the value of version, but believes that the head can be slowly and gently turned with the forceps successfully in most of these cases. He urges that as little force as possible be used in this delivery. Should efforts fail, craniotomy should be done. When the head is oblique he believes that two applications of the forceps will be usually necessary, but when the head extends transversely he believes that one will be needed. In these cases the straight forceps has a decided advantage in obtaining a better traction in the axis of the pelvis.

GYNECOLOGY.

UNDER THE CHARGE OF

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ASSISTED BY

WILLIAM E. STUDDIFORD, M.D.

Artificial Sterilization.—Kocks (*Centralblatt für Gynäkologie*, 1902, No. 37) describes a method of preventing conception in women with certain chronic affections, suggested to him by the obstruction to the passage of the spermatozoa caused by a small mucous polypus in the cervix. He dissects off flaps of cervical mucous membrane, anterior and posterior to the os externum, and allows them to hang down so as to close the os, suturing the raw surfaces at their bases. These form together a sort of valve, allowing menstrual flow and secretions to escape, but opposing the entrance of spermatozoa.

Influence of the Gonococcus in Pregnancy and the Puerperium.—Fruhinshalz (*Annales de Gyn. et d'Obstétrique*, November, 1902) emphasizes the fact that the lochial discharges furnish the most favorable medium for the development of the gonococcus. In fact, it is often found for the first time after delivery, having been overlooked during pregnancy, without any possibility of fresh infection. Mixed infection is rare, as the gonococcus does not thrive in the presence of other microbes. On the other hand, gonorrhœal infection often favors the development of the streptococcus and staphylococcus.

Hence, parturient women with pre-existing gonorrhœa are exposed to the danger not only of the lighting up of the old trouble, but to the extension of the acute inflammatory process to the adnexa and peritoneal cavity.

Treatment of Cancer of the Uterus.—Pozzi (*Annales de Gyn. et d'Obstétrique*, November 1902) concludes a paper on this subject, read before the International Congress, with the following deductions: 1. The surgical treatment of uterine cancer rarely results in a permanent cure, the average period of freedom from recurrence in the most favorable cases being from four to six years. 2. Hysterectomy is not justifiable in cases in which the uterus is fixed by extension of the disease to the surrounding tissues; curettement and cauterization give the best results under these conditions. 3. The importance of involvement of the glands has been exaggerated. Recurrence nearly always takes place in the cicatrix. Extirpation of the lymph nodes can never be complete, and seems to have no influence on recurrence, therefore, the abdominal route should not be chosen with this object alone. 4. Abdominal hysterectomy is more dangerous than vaginal, and there is a greater risk of infection, hence it should be reserved for cases in which the indications are clear—large size of uterus, adhesions, narrow

vagina, etc. 5. In early cases of uterine cancer vaginal extirpation gives excellent results, while in advanced cases palliative treatment is preferable. 6. Vaginal hysterectomy is then the operation of election in cases in which the uterus is movable and there is no palpable evidence of extension of the disease to the surrounding tissues, with such exceptions as have been mentioned.

Jonnesco, in discussing this paper, takes the optimistic side of this question. He concludes that the results of the surgical treatment of uterine cancer are quite satisfactory, since life is prolonged and a radical cure is sometimes obtained. The ideal operation is one that includes complete removal of the uterus and adnexa, of the pelvic connective tissue, the vessels and lymph nodes, the iliac and lower lumbar, as well as the pelvic. This cannot be accomplished by the vaginal route, which should be reserved for partial or palliative operations. Abdominal hysterectomy should be limited to cases in which a radical operation is possible, that is, at an early stage in the disease.

Wertheim agreed with the last speaker, and reported 120 cases of complete abdominal extirpation, with a former mortality of 20 per cent., now reduced by better technique to 13 per cent. In his first series, in which over two and one-half years had elapsed since the operation, 77 per cent. of the patients were cured, as compared with 56 per cent. reported by Chrobak after vaginal hysterectomy. Careful examination of the extirpated glands in 80 cases showed that these were cancerous in 48, which fully justified radical extirpation.

The majority of the speakers favored the radical operation.

Herpes of the Larynx during Menstruation.—Bettmann (*Berliner klin. Wochenschrift*, 1902, No. 36) reports a case in which an herpetic eruption on the laryngeal mucous membrane appeared only during the menstrual period. Herpes of the lips or external genitals is most commonly observed, though this menstrual eruption has been rarely seen on the hands, neck, or lumbar region, or even on the breast. Isolated cases have been reported in which vesicles appeared on the portio vaginalis or vaginal mucosa. The cause of this phenomenon in unknown, but it is probably of reflex nervous origin.

Uterus Duplex Separatus.—Paner (*Centralblatt für Gynäkologie*, 1902, No. 25) reports the case of a girl, aged eighteen years, who was operated upon for supposed tumor of the left ovary, accompanied by severe local pain and dysmenorrhœa. On opening the abdomen the enlargement was found to be a hæmatosalpinx attached to a rudimentary uterus which was distended with blood. There was no communication with the cervix. It was extirpated, the normal uterus and right adnexa being preserved. The patient made a good recovery and menstruated without pain ten days after the operation.

Malignant Folliculoma of the Ovary.—Gottschalk reported to the Berlin Medical Society (*La Gynécologie*, 1902, No. 4) a case of tumor of the ovary the size of the fist, which presented considerable interest. It was of firm consistence, and was surrounded by a capsule which represented the

tunica albuginea. On section a cortical and a medullary zone could be distinguished, the former containing small cysts, the latter being solid.

Microscopically the growth showed a stroma of hyaline tissue with numerous hemorrhagic foci. The cells in the parenchyma were multinucleated and were arranged in groups without capsules, often as the lining epithelium of small cysts. The tumor resembled an aberrant thyroid. The reporter believed that the epithelial elements developed from the primordial follicles.

Pulmonary Embolism Following Hysterectomy.—PICHEVIN (*Semaine Gynécologique*, June 17, 1902) collected 586 cases of hysterectomy for uterine fibroid, with a total mortality from pulmonary embolism of 2 per cent. Vaginal hysterectomy for the same condition was attended with a mortality of 3.35 per cent. from embolism, and myomectomy with one of 12 per cent.

The writer believes that the veins may be thrombotic before as well as after operation.

Death may occur suddenly on the third day after operation, though in one instance it took place on the twenty-sixth day. It is usually unexpected, and is often unattended with any elevation of temperature.

Phlegmasia, though not a positive contra-indication to operation, renders it more dangerous.

Parotitis after Ovariotomy.—PICHEVIN (*Semaine Gynécologique*, June 17, 1902) points out the fact that this complication was regularly noted by the older writers in from 2 to 10 per cent. of their cases. It has become quite rare since the introduction of modern aseptic technique. Parotitis may be due either to the extension of inflammtion from the mouth along the duct of Steno, or it may represent a local manifestation of a general infection, the latter being more probable. Parotitis prolongs the convalescence, and may result fatally. The use of an antiseptic mouth-wash, preferably a solution of chloral, is recommended.

Turpentine in Metrorrhagia.—LIENEVITCH (*Meditz. Obozreiné; La Gynécologie*, August, 1902) has used this drug for several years in cases of uterine hemorrhage, with satisfactory results. Having dilated the cervical canal, if necessary, he introduces into the uterine cavity a strip of gauze soaked in purified turpentine. It is left *in situ* for six or eight hours, being removed if the pain becomes severe. No ill effects have been observed.

The writer has found this treatment best adapted to cases of interstitial fibroid, climacteric hemorrhage, and to those in which metrorrhagia recurs after curettement.

After-effects of Supravaginal Amputation for Fibroid.—THOMAS (*Lancet*, 1902, No. 5) reports the result of his observations in the cases of 101 patients who were kept under observation for five years after operation. All the patients were benefited. No tendency to mental aberration was noted, though in a few instances there was slight loss of memory. There were no disturbances of the bladder or bowels, nor any after-pains. As a rule sexual feelings were preserved. The writer's experience has confirmed his belief as to the importance of preserving one ovary after removal of the uterus.

Ovarian Tumors Complicating Pregnancy.—PÜRCKHAUER (*Inaugural Dis.; Abstract in Centralblatt für Gynäkologie*, 1902, No. 32) analyzes reports of twelve cases from Hofmeier's clinic, with the following conclusions: An ovarian tumor complicating pregnancy must be regarded as an ever-present danger for both mother and child. 2. Ovariotomy is always indicated, and the prognosis is good even if peritonitis has already developed. 3. Abdominal section should be performed at once if a cyst ruptures during labor. 4. If for any reason ovariotomy is contraindicated during pregnancy, it should be performed as soon as possible after delivery.

Retro-peritoneal Lipoma and Uterine Fibroid.—ULLMAN (*Hygeia; Centralblatt für Gynäkologie*, 1902, No. 15) reports the case of a patient, aged forty-six years, who had an abdominal tumor of seven years' standing. On palpation obscure fluctuation was noted. After opening the abdomen an enormous retroperitoneal lipoma was found (eleven pounds), which was removed in fragments, adhesions in the neighborhood of the right kidney being separated with difficulty. It seemed that the growth had developed from the perinephritic fat. Hemorrhage was moderate. A uterine fibroid, the size of the fist, which had undergone calcareous degeneration, was not disturbed.

Ethyl Chloride in the Treatment of Incurable Cancer.—BRAMON (*Arch. de Méd. et de Chir. Spec.; La Gynäkologie*, April 15, 1902) speaks highly of the following method of treating inoperable cancer of the uterus and vagina, adopted by Horwitz: A few days after curettement and tamponade with gauze the spray is applied to the diseased surface for from one to five minutes, or until it has been blanched several times. The treatment is repeated in three days, and is continued subsequently at longer intervals. Healthy granulations form, and in time new epithelium develops. The patient's general condition improves and menstruation becomes normal. The writer has observed that under this treatment a uterus which had previously been fixed may become movable, probably due to the absorption of inflammatory exudate.

Ligation of Internal Iliac and Ovarian Arteries in Cancer of the Uterus.—KRÖNIG (*Centralblatt für Gynäkologie*, 1902, No. 41) recommends this operation in inoperable cancer of the uterus, and reports three successful cases. The operation can be done quickly, with no loss of blood, and the convalescence is rapid.

He ligates both internal iliacs at their origin with silk, and ovarian arteries at their points of entrance into the broad ligaments. In order to prevent the formation of a collateral circulation the round ligaments should also be tied. A transverse abdominal incision may be made midway between the symphysis and the umbilicus.

In the three cases reported the hemorrhages were promptly checked, but in five discharges were only temporarily lessened. The writer believes that this operation is indicated in all cases in which after opening the abdomen radical extirpation of the cancerous uterus is contraindicated, since there is no added risk.

OPHTHALMOLOGY.

UNDER THE CHARGE OF

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Etiology of Myopia.—Prof. Widmark, Stockholm (*British Medical Journal*, November 1, 1902), criticises the commonly accepted view that convergence is the most important factor in the origin of myopia. His criticism of the theory of convergence is based upon the following thesis, which he thinks his observations warrant: If by any cause the sight of the one eye is weakened in early childhood, myopia is developed exclusively or principally in the other (strong) eye, whether the first-named takes part in fixation or passes on to convergent or divergent strabismus. If one of the eyes is lost a typical myopia may be developed in the remaining eye. He thinks the chief cause of myopia is "seeing" in a limited sense—*i. e.*, perception in the retina, particularly in the yellow spot and the processes connected therewith at the posterior pole of the eye. Whatever these processes may be, the effort of discerning objects quickly following each other, as in reading or writing, might lead to hyperæmia, which may become a predisposing cause of the myopic changes at the posterior pole. Based upon this view, myopia is to be prevented only by facilitating the work of the retina. Correcting glasses are the most useful means at our command, not by lessening the pressure of the muscles of the eyeball on any of the vertex veins, or by lessening the strain on the optic nerve at the posterior pole, but chiefly by facilitating binocular fixation, and thus contributing to a clear image of the fixed object at the fovea. Moreover, correcting glasses improve the position of the body during near work and increase the distance for accommodation.

The Course of the Fibres in the Optic Nerve as Shown by Their Degeneration after Experimental Lesions of the Retina.—Parsons, London (*British Medical Journal*, November, 1902), produced in the retinæ of monkeys lesions with a Graefe knife, 1 to 3 mm. long, transverse to the general direction of the nerve fibres, in different quadrants of the retina. Two to three weeks later the animals were killed; the eyes, optic nerves, and brain were prepared and examined, with the following results:

1. The degenerated fibres in the main retain the same position along the whole course of the nerve; that is, the nasal fibres keep to the inner side of the nerve, and the temporal to the outer side. There are usually some outlying fibres degenerated, probably due to the operative disturbance of the vitreous.

2. There are invariably some degenerated fibres in the optic nerve of the opposite side. This result confirms the previous experiments of Pick, and of Dean and Usher on the rabbit by the ordinary Marchi method. These fibres tend to occupy the homonymous side of the opposite nerve. They are probably collaterals of the fibres in the nerve of the injured side, and are, perhaps, distributed to physiologically corresponding parts of the opposite retina.

3. The fibres from the macular region pass from the temporal side of the nerve anteriorly toward the centre as they pass back.

4. In all cases there is degeneration in both optic tracts. The degeneration in the opposite tract in temporal lesions is slight, but definite. As far as the method is capable of showing it consists of fine fibres, probably collaterals of the fibres in the nerve of the injured side.

5. The fibres spread out as they pass back in the tracts, and are distributed over their whole area posteriorly. Most go to the external geniculate body, some to the optic thalamus, and a few to the superior corpus quadrigeminum.

6. In many cases there was apparent degeneration among the fibres of the roots of the third and fourth nerves. These were probably fatty globules in lymph channels, as in some of Marchi's early experiments, and not true degenerations.

The Immediate Treatment of Wounds of the Eye.—Snell (*Quarterly Medical Journal*, May, 1902) remarks upon the importance of prompt treatment of wounds of the eyeball and lids. The importance of early treatment is especially shown in wounds implicating the edges of the eyelids. Neglect may result in more or less deformity. When the eyeball is wounded thorough cleansing of the outside, as well as the inside, with sublimate or other antiseptic solution is essential. A simple and efficient irrigator is a pledget of cotton-wool saturated with the solution. Sympathetic ophthalmia seems to be less frequent in recent years than formerly; this happy result may be justly ascribed to the use of antiseptics and the immediate treatment of injuries.

Clean-cut wounds of the cornea usually heal readily if the iris is not engaged therein. The more important cases are those in which the iris has become prolapsed or entangled. These require immediate treatment. The method formerly in vogue was to leave the prolapse alone, but this means frequently a protracted recovery at the best, and not infrequently, unfortunate results ensue, even at a remote period. Among these may be mentioned recurring irritability of the eye, with gradual loss of any vision at first recovered, increased tension (secondary glaucoma), and sympathetic mischief in the fellow eye, especially if the injury has involved the ciliary region. The attempt should be made to replace the prolapsed iris or to clear the wound of any entangled portion by means of a spatula. If this proves ineffectual, as it often will, the prolapsed portion should be incised. It is more difficult to remove a part of the iris when it is merely entangled in the wound. It is often necessary to excise a portion, first from one lip of the wound and then from the other. Following this atropine is usually better than eserine, unless the wound be toward the periphery. It is especially

important to remove a part of the prolapsed or entangled iris if the wound encroaches on the ciliary region. In wounds of the sclera the writer advocates suturing the conjunctiva over it. The sclerotic wound becomes thus a subcutaneous one. If a foreign body is lodged in the eye or a traumatic cataract has been produced treatment in the first instance must have regard to those conditions.

The Cortical Centres of Vision as Demonstrated after Enucleation or Atrophy of the Eyeball.—GALLEMAERTS (*Bull. de l'Acad. Royal de Méd. de Belgique*, vol. xvi., No. 4) formulates the following conclusions: 1. After enucleation or atrophy of one eyeball the fact that partial decussation of the nerves takes place is demonstrated by atrophy of certain cells in both occipital lobes. 2. This cellular atrophy is more pronounced on the side opposite that of the missing eyeball. 3. The atrophy is especially limited to the region of the calcarine fissure, the lingual lobe, and cuneus, involving these parts to an extent varying in different subjects. 4. The visual zone is limited to the region of the calcarine fissure, the lingual lobe, and the cuneus. It occupies neither the descending gyrus nor the fusiform lobe, and still less the angular gyrus. 5. All the cellular layers of the visual zone participate after the lapse of a certain time in the atrophy. 6. The ribbon of Gennari or Vicq d'Azyr cannot be considered as an exclusively optic region.

Treatment of Ophthalmia Neonatorum.—FROMAGET (*Journal de Méd. de Bordeaux*, 1902, No. xix.) observes that this disease with the vague and inexact name may be caused by the streptococcus, the pneumococcus, and many other species of microbes, but the gonococcus is the commonest and most dangerous. This ophthalmia is at first a purulent conjunctivitis. The cornea is never primarily diseased, but only as a complication. This complication does not occur in skilled hands when the disease is treated from the beginning. When the cornea does become involved the worst results are to be feared. Every case properly treated from the beginning should recover without corneal involvement.

[This statement is rather too sweeping. It unfortunately occurs, though happily rarely, that the cornea does become involved in spite of prompt and proper treatment.—ED.]

There are two indications for the physician and midwife: 1. Prophylaxis. 2. Efficient treatment from the beginning. As regards prophylaxis, the principal obstacle is the obstinacy of many midwives and even physicians in refusing to recognize the danger. They consider the reddening eyes to be "only a cold" which will get well of itself. A terrible catastrophe is necessary to drive the lesson home.

In the treatment nitrate of silver is sometimes abused. This agent is not only an antiseptic, but also a caustic. Strong solutions frequently repeated may injure the corneal epithelium. The whole treatment is directed against this very thing. By all means avoid every injury of the corneal epithelium. It is surprising to observe the resistance which the epithelium of the cornea offers to the infection; how, though bathed in pus, it preserves its precious lustre, which seems to defy the attacks of the disease; but let there occur

the slightest solution of continuity, the smallest chemical or physical wound, and the infection invades the transparent membrane whose protecting cuirass is broken. An essential part of the treatment consists in ridding the conjunctival sac of pus. The pus adherent to the lids is first washed off, and the retained pus is expelled by gently opening and closing the lids. This constitutes the external toilet, which can be done by anyone. It is to be followed by lavage of the conjunctiva, a therapeutic measure of prime importance. Permanganate of potash in 1 per cent. solution, subsequently reduced to 0.50 or 0.25 in boiled or borated water, is as good as any medicament for the purpose. This solution is neither irritating nor painful, like formalin or sublimate, and its germicidal quality is well known. It does not injure the cornea. The discoloration of the skin caused by it can be removed by solution of bisulphide of soda, 10 or 20 per cent. To properly irrigate the conjunctival sac the lids must be separated by the hands if the œdema is not too great. The child's head must be immobilized; one or two assistants may be necessary. If the lids cannot be properly separated by the fingers, lid retractors should be used, so that the whole conjunctiva may be given an antiseptic bath. Sterilized tampons of absorbent cotton are dipped in the warm solution and squeezed, so that the liquid flows over the whole sac. Rubber bulbs and syringes may also be used, but with these great care is necessary to prevent splashing into the attendant's eye. There is no such danger with the tampon. If retractors are used they should only be employed by an experienced hand, otherwise the corneal epithelium may be scraped. How abundant should these washings be? Should litres be poured over the conjunctiva? Not at all. When the sac has been thoroughly cleansed of pus and the liquid flows out clean, more is useless and may be dangerous from positive injury of the cornea by the instruments. After the conjunctival baths the lids are to be carefully turned back and the swollen conjunctiva lightly sponged with warm tampons to remove the false membranes which result from the coagulation of purulent masses. The washings should be made each time before the child nurses. After-improvement begins every four or five hours, subsequently at longer intervals. These irrigations are very important, and certain benign cases are greatly improved thereby, but they cannot assure recovery alone.

An agent capable of affecting the pathogenic microbes, even when in the epithelial cells, is to be brought upon the surface of the palpebral and ocular conjunctiva. This agent is nitrate of silver. Many oculists recommend its employment in strong solutions—2 and 3 per cent. Precaution must be taken to avoid injuring the cornea by the caustic. A solution of chloride of sodium should be used to thoroughly neutralize any excess of silver. If so used the conjunctiva is cleansed as above described, the upper lid being completely everted is painted with the silver, the lower remaining in position to protect the cornea. The upper lid is to be turned back before proceeding to cauterize the lower; but this plan has one element of danger, namely, the risk of injuring the cornea, notwithstanding every precaution. The writer, therefore, recommends cauterization by means of the solid stick. This only reaches the spots intended. It dissolves slowly enough, so that it can be quickly neutralized. The cauterizations are to be repeated daily until the subsidence of the inflammation, as shown by the diminution of the

œdema and the ability of the child to open its eyes. As the stick cannot reach the cul-de-sac and deep folds, the cauterization is to be followed by a large instillation of a 1 per cent. solution of nitrate of silver, seven or eight drops. This is free from danger, and can be used by any physician or capable nurse. In cases treated from the start and all mild ones such instillations repeated twice daily suffice without the use of the stick. When the child for any reason cannot be seen by the physician, weak solutions, 0.01 to 0.05 per cent., can be used by the nurse three times a day, following irrigation with permanganate. The stick is to be reserved for severe cases with great œdema and profuse suppuration.

The crux of the treatment is the irrigation. The difficulty is to have this properly performed. Efficiency without violence is the secret. When the pus has disappeared the silver may be replaced by astringent collyria of sulphate of zinc. The strength of the permanganate is to be reduced and finally replaced by borate of soda in solution. The eye should never be bandaged. The outflow of pus is to be favored and not restrained. The margins of the lids may be oiled with an ointment of simple vaseline or yellow oxide of mercury or aristol. Iodoform is to be avoided, being frequently an irritant.

PATHOLOGY AND BACTERIOLOGY.

UNDER THE CHARGE OF

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On the Pathological Changes in Hodgkin's Disease, with Special Reference to its Relation to Tuberculosis.—Dr. Dorothy M. Reed (*Johns Hopkins Hospital Reports*, 1902, Nos. 3, 4, and 5, vol. x. p. 133) states that since Hodgkin first described, in 1832, the peculiar enlargement of the lymphatic glands, the exact nature of the pathologcal changes in the glands and the cause of their lesions has been the subject of much discussion. At various times the disease has received different synonyms. Progressive multiple gland hyperplasia (Wünderlich, 1858), lymphosarcoma (Virchow, 1864), pseudoleukæmia (Cohnheim, 1865), adenia (Trousseau, 1865), and malignant lymphoma (Billroth) have all been used to designate this affection. Delafield, in 1887, reported a case of primary tuberculosis of the lymph glands simulating pseudoleukæmia, and other authors have made similar observations. Sternberg found tuberculosis in eight out of thirteen autopsy cases

of Hodgkin's disease, and concluded that the lesions in the glands were due to a peculiar tuberculous process. Clarke finds no warrant for the assumption that the process is a tuberculous one.

Two etiological possibilities have heretofore been considered, viz., that of a malignant growth and that of an infectious process. So far the bacteriological findings have been entirely unsatisfactory, but although the histological changes resemble somewhat those of a new-growth, the author believes that further investigation will show a great similarity to inflammatory processes. Tuberculosis has been considered the cause of Hodgkin's disease by several observers. With this view the author entirely disagrees, for although tuberculosis may exist at the same time with Hodgkin's disease, the two processes are totally distinct. In most of the cases when both affections coexist, tuberculosis appears as a secondary process.

Clinically the disease can be easily recognized. It occurs oftenest in early life, and much more frequently in males than in females. A tuberculous family history is not found in an unusual percentage of cases. Throat trouble and inflammation of the eye or ear often precede the growth. The one constant feature is a progressive enlargement of the lymphatic glands, usually beginning in the cervical nodes, and being at first unilateral. The single large glands can often be mapped out, and involvement of the skin or adjacent tissues rarely occurs unless there is secondary infection. Progressive asthenia, anæmia, and cachexia supervene. Other than the anæmia there are no specific blood changes. Irregular or continuous fever is the rule. Enlargement of the spleen is always present, and it may be enormous. The liver is less often enlarged. Pressure symptoms are common. The majority of cases last from one to four years, but the process may be of an acute nature.

No therapeutic measure is known which influences the course of the disease, and after extirpation of the glands recurrence is the rule.

The author reports eight cases of Hodgkin's disease, seven of which were in boys under seventeen years of age and one in a woman, aged fifty-five years. The duration of the growth varied from two to seventeen years. In all the cases there was anæmia, but otherwise the blood changes were not remarkable. All of the cases showed a slight, irregular fever, with occasional exacerbations. Tuberculin was given in five cases, but without reaction. Complete excision of the tumor mass was performed in five cases. In three cases the material was obtained from autopsies. In one of these cases there was generalized miliary tuberculosis; in the other two there was no sign of tuberculosis, and no tubercle bacilli could be demonstrated in sections from the glands. Macroscopically, the glands are discrete, and on section appear uniformly semitranslucent gray or broken by yellow streaks. The so-called metastatic nodules may appear in any organ where lymphoid tissue is found normally.

Microscopically, the earliest change in the lymph glands was an increase in the lymphoid elements, with beginning proliferation of the reticular endothelial cells. Later, the process was characterized by an extensive proliferation of the endothelial cells, from which large numbers of giant cells were formed, and the production of connective tissue, so that in the older glands the normal structure was completely destroyed. Usually eosino-

philes were present in large numbers, and plasma cells, "kugelzellen," endothelial phagocytic cells, and mast cells were also seen.

In the metastatic nodules the same series of changes take place, with the production of connective tissue and the presence of the different cells found in the lymph glands.

The conclusions are:

1. We should limit Hodgkin's disease to designate a clinical and pathological entity, the main features of which are painless progressive enlargement, usually starting in the cervical region, without the blood changes of leukæmia.

2. The growth presents a specific histological picture—not a simple hyperplasia, but changes suggesting a chronic inflammatory process.

3. The microscopic examination is sufficient for the diagnosis. Animal inoculation may confirm the decision by its negative results.

4. Eosinophiles are usually present in great numbers in such growths, but not invariably. Their presence strengthens the diagnosis.

5. The pathological agent is as yet undiscovered. Tuberculosis has no relation to the subject.—W. T. L.

Report on Diphtheria Bacilli in Well Persons (*Journal of the Massachusetts Association of Boards of Health*, July, 1902, by a committee of the Board working in co-operation with a number of recognized experts).—In all 4250 healthy individuals were examined in various parts of the United States, and it was found that in nearly 3 per cent. of these persons true diphtheria bacilli were found, using as a basis of judgment the three types of B. diphtheriæ described by Wesbrook. As tested on guinea-pigs, about 17 per cent. of these true forms were found to be virulent. In healthy persons who have the B. diphtheriæ as a result of exposure to the disease the percentage of virulent forms is much higher, and in such cases the persons, although themselves immune, should be regarded as fully as dangerous to the public health as convalescents from the disease. It is concluded that it is impracticable to isolate well persons infested with diphtheria bacilli if such persons have not been recently exposed to the disease; and, furthermore, it is not advisable, as a matter of routine, to isolate from the public all the well persons in infected families, schools, and institutions.

On the Cultivation of the Virus of Variola.—T. Ishigami (*Sei-I Kwai Medical Journal*, Tokyo, 1902, vol. xxi., Nos. 4 and 5) has been able further to identify the protozoon described by Guarnieri as the cause of vaccinia and variola, and also to cultivate this organism on a bouillon medium containing the epithelial cells of normal calves. That this is the true etiological factor in variola he has shown by reproduction of the characteristic lesions in calves by inoculations with cultures transplanted as far as the third generation. The protozoon resembles in its life cycle the microsporidia. It occurs in variola lymph, in scabs, and in the epithelial cells of the inoculated calf, in the form of sporozoites, which, under favorable circumstances in the animal, develop by direct division into cysts. In culture media the growth is less rapid, and the power to reproduce the specific lesions is lost at the third transplantation.—F. P. G.

On the Sensibilizers of Sera Active against Albuminoid Substances.—GENGOU (*Annales Pasteur*, 1902, vol. xvi. p. 734) shows that the blood sera of animals immunized with cow's milk, egg-albumin, pure fibrinogen, and heated serum possess, in addition to the precipitins, which have already been described, substances analogous to the "substances sensibilisatrices" (amboceptors), which have been so much studied in the hæmolytic and bacteriolytic sera. The presence of such sensibilizing substances may be detected by their power to absorb alexins (complements) from normal sera, as is shown by the inability of such mixtures subsequently to complete the hæmolysis of sensibilized hen's red blood corpuscles. These experiments presuppose and would seem further to confirm Bordet's theory of unity of the alexin. Such albuminous sensibilizing bodies are further shown to be non-specific within certain limits, as is the case with the precipitins.—F. P. G.

The Pathology of Lymphotoxic and Myelotoxic Intoxication.—FLEXNER (*University of Pennsylvania Medical Bulletin*, 1902, vol. xv. p. 287) describes the histological changes in the blood-forming organs of the rabbit and guinea-pig when inoculated with the blood of animals previously treated with sterile emulsions of one set of these organs (lymph nodes, spleen, or bone-marrow). Funck has already noted the effect on the various forms of white blood corpuscles *in vitro* and *in vivo* when treated with lymphotoxic, myelotoxic, and splenotoxic sera obtained by immunization of another species of animal with the substance of the different blood-forming organs; but hitherto no one has described the effect produced by such sera on the organs against which the foreign animals have been immunized. Lymphotoxins, splenotoxins, and myelotoxins are found to produce a most marked effect on their respective organs, but this activity is not entirely specific, as the other sets of blood-forming organs are also affected. In brief, the changes noted are, in the case of the lymph nodes, enlargement due to hyperplasia of the germinal nodes; in the spleen, enlargement through hyperplasia of the Malpighian bodies; and in the bone-marrow an enormous increase of the white blood elements. The three toxins are distinct and different in their action, and the myelotoxin possesses a far more active effect on the non-specific organs.

This community of interaction would indicate, it appears, the existence of common receptors in all the blood-forming organs, and further investigations along this line promise to reveal a more definite basis for the understanding of the origin of the formed elements of the blood.—F. P. G.

On the Actinomyces-like Development of Some of the Acid-resisting Bacilli (Streptothrices?).—A. C. ABBOTT and N. GILDERSLEEVE (*Centralblatt für Bacteriologie*, 1902, No. 12, Band xxxi. p. 547), experimenting with the grass bacillus II. (Moeller), the timothy hay bacillus (Moeller), and the butter bacillus (Rabinowitsch), found that after intravenous inoculations of the organisms small nodules developed in the kidneys of the inoculated animals. This occurred at the end of twelve to fifteen days, at which time the animals were killed. The lungs were rarely affected. Histologically, these nodules closely resembled tubercles, and the author's findings practi-

cally coincided with those of Hoelscher. From these areas were recovered the acid-proof bacilli injected. Certain bodies unstained by ordinary histological methods appeared in the lesions, which, on account of their rosette-like shape, suggested the structure of a mycelium. Stained by the method of Gram or Babes and Leoarditi, they were readily recognized as mycelia, strikingly like actinomyces. The typical actinomyces mode of growth was common, but beaded threads were also found closely matted together and grouped like bacillus tuberculosis grown upon artificial media. A study of this mycelial development suggested that the original bacilli were really segments of the beaded mycelial threads. Small coccus-like bodies were found about the mycelia and often extended into the surrounding tissues. These were taken to be sections of hyphæ.

Comparing the distinguishing staining reactions of this group of saprophytes with those of bacillus tuberculosis; comparing the various morphological peculiarities exhibited by some of them with those now known to occur during the life of bacillus tuberculosis—notably branching, mycelial development under artificial conditions, and actinomyces-like growth in diseased tissues—and considering the fact that one of the results of the pathogenic actions of all is the production of nodular new-growths having often many features in common, the authors regard them as botanically closely allied and as morphologically improperly classified. They therefore suggest that they be grouped with the actinomyces or the streptothrices, in conformity with the suggestions made by others concerning bacillus tuberculosis.—W. T. L.

On the Bacteriological Findings in an Epidemic of Dysentery in Southern Syria.—P. T. Müller (*Centralblatt für Bacteriologie*, Abt. 1, Band xxxi., S. 558) reports his findings in a few cases at the end of a dysentery epidemic in this locality. He regards it as distinctly proved by the researches of Shiga, Flexner, Kruse, and Vedder and Duval that epidemic dysenteries in general are universally caused by a specific micro-organism, the B. dysenteriæ—an organism which, however, may possess slight cultural variations in different localities. Müller himself isolated an organism varying in no particular culturally from the B. dysenteriæ as described by the authors mentioned. Guinea-pigs and rabbits inoculated with this bacillus, and others with the organism of Kruse, showed interagglutinations, still further demonstrating the unity of the species.—F. P. G.

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METASTATIC CARCINOMA OF THE CHOROID. WITH REPORT OF A CASE AND REVIEW OF THE LITERATURE.

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The medical history of carcinoma of the choroid commenced in 1872, when Perls,[1] the pathologist, examined the eyes of a man who had died from carcinoma of the lung, and found metastatic deposits in each choroid. No clinical history of the eye symptoms is given. As the report of this case belongs to the domain of general pathology, it apparently failed to attract the attention of ophthalmologists, as ten years elapsed before the subject again appeared in medical literature, when, in 1882, Hirschberg[2] and Schoeler[3] each exhibited a case before the Berlin Medical Society.

Although cases have occasionally been observed and reported since, carcinoma of the choroid still remains one of the curiosities of ophthalmology. It is, however, not improbable that many cases have escaped a correct diagnosis, for the reason that text-books, by practically ignoring its existence, have failed to place clinicians on the alert for its detection. The value of bearing its possible occurrence in mind is significantly shown by the fact that of the thirty authors quoted five have had two cases each to report.

The following case occurred in my own practice:

P. G., a Belgian, aged fifty-six years, carpenter; family history negative. About one year before he came under my observation a physician told him that he had saccharine diabetes. This disappeared in a few

months. He had recently suffered from indigestion and occasional asthmatic attacks. He was well nourished, and no cachexia was apparent. Eye trouble had existed for eighteen months. He first noticed a blur before the left eye. This rapidly increased, and the eye became blind in about six weeks. There was no pain whatever at this time, but about two months before I saw him he began to suffer from violent paroxysms of pain in and around the eye. The increasing frequency and severity of these attacks led him to seek medical relief.

Examination. The right eye was apparently normal in every respect. The left eye had no perception of light. Ciliary congestion was pronounced. Tension was + 1. Cornea and lens were clear. Anterior chamber shallow. The pupil was contracted and fixed by extensive posterior synechia. The ophthalmoscope and oblique illumination revealed a grayish, immovable, non-vascular mass, closely applied to the posterior surface of the lens.

This painless loss of vision, which was followed by eighteen months of quiet and the subsequent development of a rapidly progressing glaucoma, led to the diagnosis of an intraocular growth. After consultation with Dr. Neil Hepburn, an enucleation was advised. The operation was performed under ether on November 11, 1901. Extensive adhesions of the globe to the orbital tissues existed, especially posteriorly. The wound healed kindly, but the general health of the patient failed with alarming rapidity. Rapid emaciation, loss of appetite, cough, and dyspnœa ensued. A laryngological examination by Dr. Beaman Douglas showed a left abductor paralysis of the vocal cord. One week after enucleation the right pleural cavity exhibited evidence of a fluid effusion. Enlargement of the deep clavicular glands on the right side was now first observed. About this time I examined the enucleated eye microscopically, and found that it contained a carcinoma of the choroid. As this could not be a primary growth, it was at once apparent that the patient must have a carcinoma of some other organ, which was rapidly tending to a fatal termination. On November 30th the patient was referred to Dr. W. H. Porter,[4] who placed him in the New York Post-graduate Hospital, where he died December 16, 1901, about eighteen months after the first eye symptoms and thirty-five days after enucleation of the eye.

Necropsy by Prof. H. T. Brooks and Dr. R. H. Halsey, the house surgeon, showed that the primary carcinoma was situated in the liver, with secondary deposits in the choroid of the left eye, the right suprarenal body, the right and left kidneys, spleen, retroperitoneal glands, right bronchus, right lung, and bronchial glands. Within the cranial cavity tumors were found on the falx cerebri, tentorium cerebelli, and in the pia mater resting on the nates. I made numerous microscopic sections of all these deposits for comparison with the choroidal growth.

Anatomical and Microscopic Examination. When the globe was punctured, immediately after enucleation, to facilitate the process of hardening, a thin, yellowish fluid escaped, which resulted in some distortion of the specimen.*

The exterior of the globe, especially in the posterior region, exhibited evidence of the close adhesions it had formed with the surrounding

* This puncture, to allow the "fixing" fluid to enter the interior of the globe, is commonly believed to be essential in preparing eyes for histological examinations. As it often leads to distortion of the specimen, I have since abandoned it as wholly unnecessary.

tissues. The hardened eye was sectioned horizontally somewhat below the axis (Fig. 1). The entire posterior and lateral portion of the globe was lined by a grayish-white, knobby, discoid growth. Its centre, which was in the macular region, was 3 mm. in height. From this point it diminished gradually in thickness to its thin-edged periphery, which extended forward to the apex of the ciliary body on the temporal side, and about 9 mm. beyond the optic nerve on the nasal side.

The retina was completely detached, except at the ora serrata and optic nerve. Behind the retina was an albuminous coagulated mass almost, but not completely, filling the remaining space in the globe. This space of about 1 mm., which existed between the coagulum and the growth, probably contained the fluid which escaped when the puncture referred to above was made.

The growth was a papillary cyst adenocarcinoma (Fig. 2). It was composed of numerous cystic cavities, with connective tissue walls lined by superimposed layers of large cells of the glandular epithelial type, with abundant cytoplasm, large, strongly staining, oval nuclei and well-marked nucleoli. While young and closely packed together they were somewhat columnar in appearance, but wherever relieved from pressure they were large and polyhedral in shape, closely resembling those of the liver or kidney.*

At different points in the cystic cavities the epithelium had multiplied and formed branching elevations, into each of which grew a stem of connective tissue. This arborescent manner of growth presented a striking and fantastic picture under the microscope. All of the cancerous growths present in this case showed the same histological formation wherever they were deposited. Its structure and method of growth can better be understood if its development is traced from an area of fresh invasion backward to the older portions of the growth. At its thin-edged periphery a narrow wedge of epithelial cells could be seen pushing forward in the suprachoroidal space (Fig. 3). The choroid was thus lifted from the sclera entire, but its lymph channels were quickly invaded by cells. Its connective tissue framework, and especially that of the suprachoroidal space, underwent rapid proliferation and formed the carcinomatous stroma, while the enormously enlarged lymph spaces were filled with the characteristic epithelial cells. In the newer portion of the growth the cells preponderated over the stroma, but the older portions exhibited a decided scirrhous tendency. This tendency was well illustrated in the primary liver growth. Here the fresh deposits closely resembled those in the choroid, while the oldest portions were marked examples of scirrhous carcinoma. The distended bloodvessels and capillaries of the choroid with extremely thin walls remained in the stroma, but were supported by an enormously increased amount of connective tissue, throughout which the pigment cells of the choroid were scattered, indicating that the choroidal stroma had now become the framework of the carcinoma.

The presence of cells in the capillaries could not be demonstrated, the progress of invasion being along the lymph spaces; but foci frequently

* Their strong resemblance to liver cells was a subject of comment during microscopic examination before the patient's death when speculating on the probable site of the primary growth. However the extreme rarity of primary carcinoma of the liver, the absence of hepatic tumor, and the prominence of the pulmonary symptoms diverted attention from its true location.

formed in the perivascular lymph channels, and ultimately destroyed the vessel and entered its lumen.

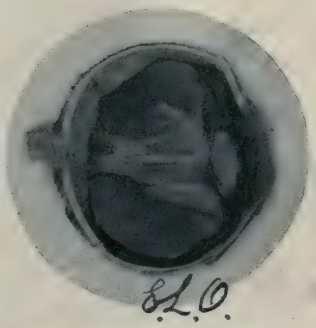
Backward toward the older portion of the growth the cystic cavities increased in size, and in some cases occupied the entire thickness of the growth. Their centres were filled by the disintegrating remains of cells and stroma, with a large quantity of grumous material staining with eosin. The latter I interpreted as the débris of dead tissue, since by careful focusing with the microscope I was usually able to demonstrate the dim outlines of cells in all parts of the mass (Fig. 2). These cystic spaces, which appear to be common in carcinoma of the choroid, have led Mitvalski[5] to evolve a theory regarding their origin. He supposes a hemorrhage to occur from obstruction. A clot forms, around which the carcinoma grows. Later on the clot shrinks and disintegrates, leaving a cystic space containing the old grumous blood clot in its centre surrounded by the carcinomatous growth. This highly ingenious theory has no application to the case under consideration. My reasons for this assumption are that the débris was not composed of blood, the potassium ferrocyanide test failing to show the presence of blood pigment. The growth was cystic from the very first, not only in the eye, but in every other organ where metastases were deposited. These large spaces containing débris occurred only in the eye-deposit. In all of the other organs the tendency was for the spaces to decrease in size in proportion to the amount of stroma.

Considering the frequency of this formation in choroidal carcinoma, it is probable that an explanation must be looked for in the anatomical structure of the eye. As stated above, there is a tendency in all of the deposits in this case to become scirrhous. In the liver, for instance, the dead cells are easily absorbed and removed, leaving no obstacle to prevent the obliteration of the cavity by connective tissue. Other conditions, however, prevail in the eye where, with its dense sclerotic coat and with its efferent vessels enveloped in a carcinomatous mass, the absorption and removal of the free cells and cast-off tissues is necessarily a difficult matter; indeed, it is probable that their accumulation, to which constant accessions are being made, will account for the large spaces which have attracted the attention of observers. Hemorrhages were not common, and apparently played but a small rôle in the process of cell necrosis. Such blood pigment as was revealed by the potassium ferrocyanide test was usually found in the stroma. Large hemispherical colloid bodies, apparently springing from the lamina vitrea, were very numerous in the choroid in front of the area of invasion, and were sometimes found also on the surface of the tumor. These bodies were similar in all respects, except their unusual size, to those ordinarily observed in degenerated eyes.

Sclera. Wherever a lymph channel was accessible to the cells the latter immediately entered and established a colony. Thus they invaded the sclera and formed many deposits among its fibres. Posteriorly was a deposit 1 mm. in height entirely outside of the sclera, but between it and the intraocular growth the sclera was so infiltrated with cells and cell nests that this deposit may be regarded as the result of perforation. This tendency of intraocular carcinoma to grow backward and to perforate the sclera by infiltration through its fibres distinguishes it from sarcoma, which almost always manifests a tendency to emerge from the globe along some of the natural openings by bursting through the

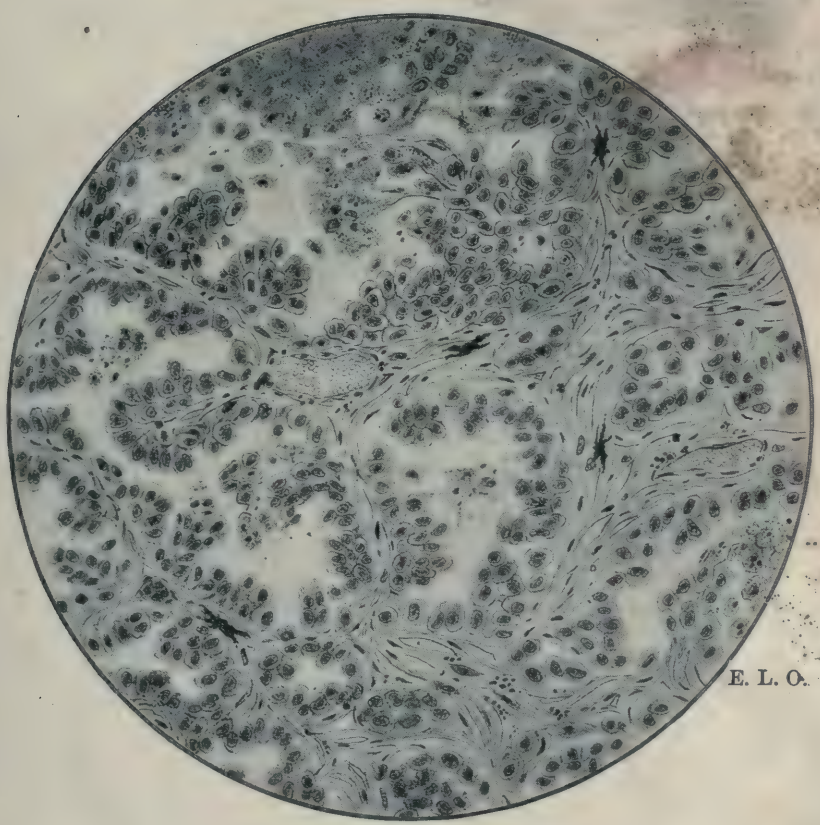
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FIG. 1.



Metastatic carcinoma of the choroid. Lower half of left eye. Horizontal meridinal section, somewhat below the axis. Actual size. (From an original drawing by the author.)

FIG. 2.



Papillary-cyst-adenocarcinoma of the choroid. The stroma contains the bloodvessels and scattered pigment cells of the choroid. The large alveolus above is filled with disintegrating remains of tumor elements. × 500. (From an original drawing by the author.)

FIG. 3.

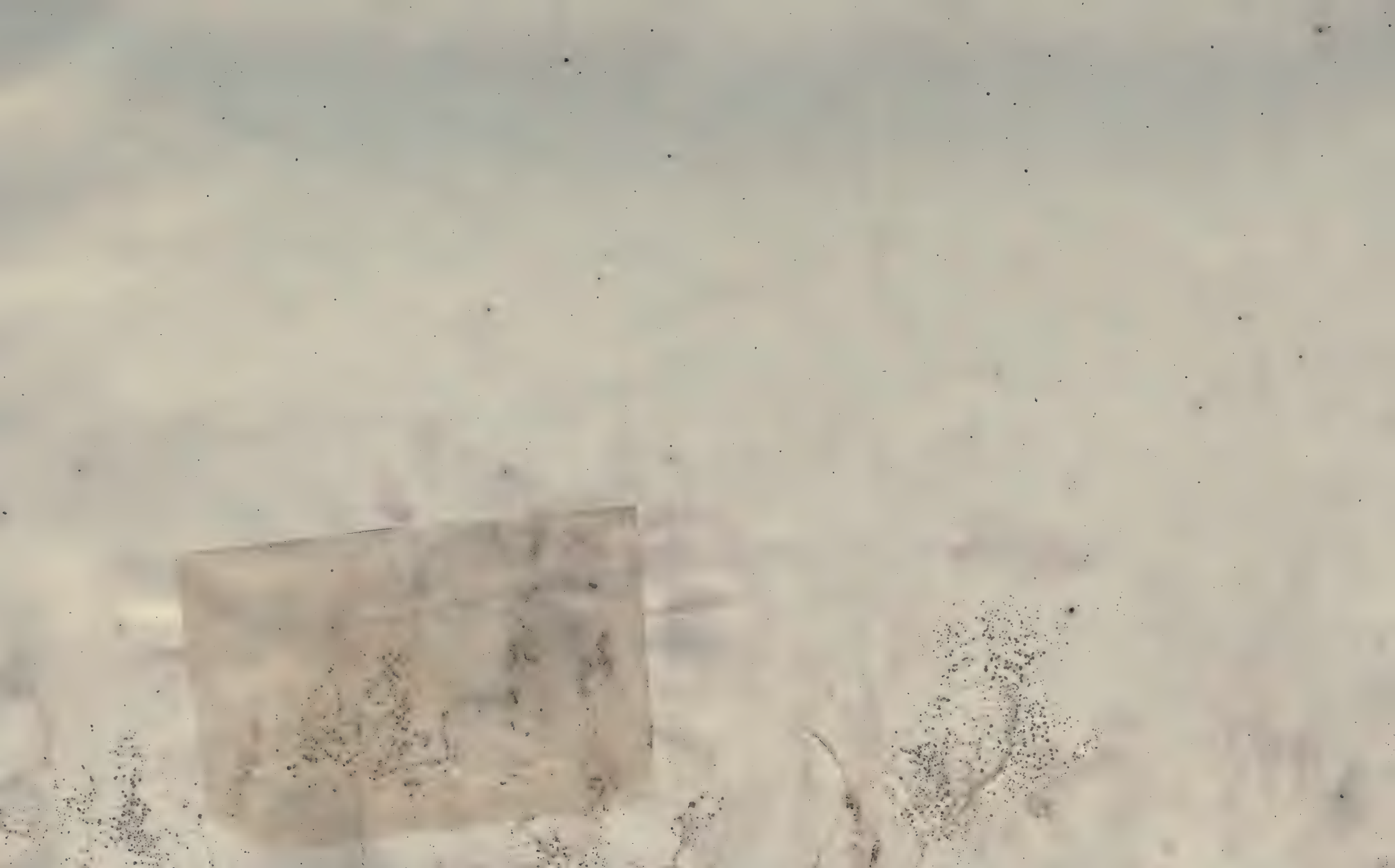


The carcinomatous growth has re ed the ora serrata. Its wedge-like periphery is advancing along the suprachoroidal space. Choroid is lifted and its lymph channels inv l. Retina totally detached, its pigment layer remains on surface of growth. Spherical colloid body beneath the pigment. × 100. (From an original drawing by the author.)

FIG. 4.



Carcinomatous invasion of optic nerve and retina. Degenerated fibres of detached retina form a stroma for the carcinomatous deposit. × 100. (From an original drawing by the author.)



vena vorticosa, the posterior ciliary arteries, or by following the lymph channels around, and in the optic nerve.

At one point a narrow deposit perforated the sclera obliquely, just where a short ciliary artery might enter. I was inclined to believe that this was the channel by which the metastasis entered, but as no remnant of vessel walls could be made out I was unable to assert this for a fact. These extrascleral deposits permitted the cells to enter the lymph spaces beneath Tenon's capsule and to migrate forward and attack the sclera anteriorly from the outside (Fig. 3).

Optic Nerve. Atrophic, and presenting the usual changes of an ascending degeneration. For a distance of 2.5 mm. from the globe it contained numerous scattered carcinomatous deposits located among the nerve fibres. After death the stump of the optic nerve, optic tracts and chiasm were removed and carefully examined microscopically, but no evidence of carcinoma could be found. This corresponds with the other histories, recurrence of the disease at the site of operation not having been observed in any of the reported cases.

Retina. The detached retina, which was drawn forward from its attachment at the papilla into a leash of thickened neuroglia and nerve fibres, contained many carcinomatous deposits (Fig. 4). Both here and in the optic nerve the proliferation of the neuroglia furnished the stroma. This was beautifully illustrated by Van Gieson's stain, which rendered the retinal stroma brown, while in the choroid and sclera the stroma had the shining red color of connective tissue.

Where detachment had occurred the pigment layer remained with the choroid, and subsequently covered the surface of the growth (Fig. 3).

Vitreous. No remnant of the vitreous remained anterior to the retina. Between the lens and the detached retina, however, was a crumpled structureless membrane which was probably the empty hyaline sac and remnants of vitreous bands. This was the gray mass observed with the ophthalmoscope during life.

Iris and Ciliary Body. The iris showed the usual changes of plastic iritis, with extensive posterior synechiæ. The filtration angle was narrow, and the region of Schlemm's canal was closely packed with round cells. The near approach of the invading elements had excited the greatest activity in the ciliary body, as shown by the engorged bloodvessels, proliferation of connective tissue elements, and round-cell infiltration.

Cornea. Clear and free from pathological changes.

Lens. Normal, except the capsular thickening at the point of iritic adhesions.

Perhaps our subject cannot be better presented than by first submitting the following extracts from published cases, followed by such conclusions as we are able to draw from their analysis. Thirty-four cases have been collected that justly or unjustly can lay claim to be considered in a review of this subject. As we consider four of them open to doubt, they have not been included in the list of cases, but are discussed in separate abstracts.

Case 1.—M. PERLS[1] (Giessen). Male, aged forty-three years. *Primary growth*—carcinoma of right lung; pain in lung for three months. Cachectic. Left eye first affected, then right eye. No operation. Cause of death, carcinomatosis; probably the immediate cause was cerebral metastases. *Autopsy*—metastases in liver, brain, and other organs. *Anatomical and microscopic examination of the eye*—nodular thickening of both choroids posteriorly; more advanced in O. S.; medullary carcinoma; choroid formed stroma for carcinoma; found carcinomatous cells in chorio-capillaris; right retina detached and perforated by small deposits. *Remarks*—published as case of carcinoma of the lung. Eye history not given. Became delirious and died twenty-four days after coming under observation.

Case 2.—J. HIRSCHBERG[2] (Berlin). Berlin Medical Society, 1882. Female, aged thirty-three years. Had carcinoma of right breast nine years before. Right eye first affected, then left eye. O. D. vision lost very rapidly. O. S. became blind in three months. *Ophthalmoscopic appearance*—O. D., yellowish thickening around nerve, 2 mm. high, fading into healthy fundus; O. S., same as O. D.; thickening 1 mm. high. T. N.; no pain. No operation. *Duration of life*—about seven months after first eye symptoms. No autopsy. *Remarks*—August 15, 1882, vision had been destroyed in O. D. very rapidly. September 15th, scotoma appeared in O. S. In December the patient was blind. She left the clinic and died early in the spring of 1883. Supraclavicular glands were enlarged.

Case 3.—SCHOELER and UHTOFF.[3] Berlin Medical Society, 1882. Female, aged thirty-three years. Carcinoma of left breast removed six years before. Right eye first affected, then left eye. O. D. blindness of ten weeks' duration when first seen. O. S. vision lost in about one month. *Ophthalmoscope*—O. D., detached retina. Grayish ring around nerve; swollen papilla; vessels dilated. O. S., pin-head sized; grayish-white dots infiltrating the macula; very rapid growth. O. D. T. + 1. O. S., T. N. No operation. *Duration of life*—thirteen months after first eye symptoms. Cause of death, carcinomatosis. *Autopsy*—metastases in right and left ovaries, right and left cerebral hemispheres, dura and pleura. *Anatomical and microscopic examination of the eye*—O. D., sessile tumor around papilla; O. S., same in the macular region. The diagnosis was melanotic carcinoma. The melanosis observed was probably the pigment cells of the choroid scattered throughout the growth. Carcinomatous cells were found in the blood-vessels. Deposits in right optic nerve and sclera. *Remarks*—case was exhibited at the Berlin Medical Society one week after Hirschberg's case. Schoeler saw refraction change in O. S. from —1 D. to + 1 D. in a short time. Vision fell to 8/200 in fifteen days.

Case 4.—J. HIRSCHBERG[6] (Berlin) (second case) and A. BIRNBACHER (Graz). Female, aged twenty-eight years. Carcinoma of right breast began six years before; was amputated one year before. Very cachectic. Left eye affected. Vision lost very rapidly; no P. L. *Ophthalmoscope*—detached retina; a whitish mass could be seen beneath it. T. —; no pain. No operation. *Duration of life*—two or three months after first eye symptoms. Cause of death, carcinomatosis. *Autopsy*—metastases in lungs, bronchial glands, liver, and kidneys. *Anatomical and microscopic examination of the eye*—tumor extended from papilla to beyond equator; carcinoma simplex; glandular epithelial cells; invasion of retina; finger-like projections between the fibres of the degenerated retina. The growth extended along the supra-choroidal space: scattered pigment in growth; no cells in bloodvessels. *Remarks*—the growth of the tumor was very rapid. The size given in the text is 9 mm. high by 12 mm. broad, but the illustration shows a tumor 9 mm. high by 25 mm. broad. This latter conforms more to the usual form. Enlarged supraclavicular glands.

Case 5.—V. MAKZ[7] (Frieburg). Female, aged fifty years. Carcinoma of right breast removed three months before. Very cachectic. Left eye first affected, then right eye. Vision lost very rapidly. Yellow reflex behind pupils; extensive detachment of both retinæ. O. D., T. N. O. S., T. —1; pain in O. S. Punctured eye to relieve the pain; not successful. *Duration of life*—ten weeks after first eye symptoms. Cause of death, abdominal metastases. No autopsy. *Remarks*—clinical diagnosis only, but case was undoubtedly genuine. The first eye symptom was a central scotoma ("cloud"). When O. S. was punctured to relieve the pain a thin, yellowish fluid escaped. No relief followed.

Case 6.—A. SCHAPRINGER[8] (New York). Female, aged fifty-one years. Adenocarcinoma of right breast amputated two years before. Left eye affected. Vision lost very rapidly. The eye appeared normal externally; pupil slightly dilated, with no reaction to light; media clear; *Ophthalmoscope*—œdema of papilla; in the macular region a reddish-white infiltration; four disks in diameter; elevated + 3.5 D.; scattered pigment; eighteen days later height of tumor was + 4.5 D. T. N. No operation. *Duration of life*—four months after first eye symptoms. Cause of death, exhaustion. *Autopsy*—incomplete; found liver, pulmonary, and other metastases. *Anatomical and microscopic examination of the eye*—discoid tumor in the macular region; scirrhous carcinoma; surface flat; no nodules. *Remarks*—a bony tumor was found growing from the right temporal bone one and one-half inches above the auditory meatus. This is interesting, as in the case reported by Guende[29] four similar growths were found on the skull. Had pleurisy, with effusion.

Case 7.—JOHANN MITVALSKI[5] (Prag). In Norris and Oliver's *System*, vol. iii., p. 546, Schoebl describes this case. Female, aged forty-six years. Carcinoma of left breast amputated two years before. Good health since breast was removed. Left eye affected. Vision lost in two weeks from onset (Schoebl[32]). *Ophthalmoscope*—oval growth; three disks in diameter, extending from papilla to macula; dirty yellow color; scattered pigment; fades into healthy fundus; in two weeks there was extensive detachment of retina. T. N. later; T. — later; T + 2; glaucoma. Enucleation for glaucoma. *Duration of life*—two months after enucleation, and three and one-half months after the first eye symptoms. Cause of death, brain and lung metastases. No autopsy. *Anatomical and microscopic examination of the eye*—"shell-shaped" growth around papilla, extending to ciliary body on the temporal side; all of choroid invaded except upper and inner third; greatest thickness 2 mm.; carcinoma simplex; scirrhous type; pigment in stroma; large spaces; carcinoma spread along the suprachoroidal space. *Remarks*—Mitvalski attributes the large cystic spaces found in the growth to blocking of vena vorticosa. Then hemorrhage forms a clot, carcinoma grows around the clot, thus forming a cystic cavity. This theory is discussed in the text of the present article. Supraclavicular glands were enlarged.

Case 8.—JOHANN MITVALSKI[5] (Prag). Male, aged thirty-five years. Carcinoma of left breast; one year duration; removed seven months before. Left eye affected. Vision lost very rapidly. *Ophthalmoscope*—flat, oval deposit in the macular region; four disks in diameter; central elevation, 3 D.; dirty yellow color; whitish patches; scattered pigment. T. N. No operation. *Duration of life*—two months after the first eye symptoms. Cause of death, brain metastases. No autopsy. *Remarks*—clinical diagnosis only, but it was unquestionably a true case of metastatic carcinoma of the choroid. Enlarged supraclavicular glands.

Case 9.—GAYET[9] (Lyon). Male, aged thirty years. Primary growth; carcinoma of stomach and liver. Good health. Right eye affected. Vision lost very rapidly. Nothing apparent, but extensive detachment of retina. T. + 3; severe pain. Enucleation. *Duration of life*—very short time after first eye symptoms and enucleation. Cause of death, cerebral metastases (?). *Autopsy*—metastases in brain, lungs, liver, and stomach. *Anatomical and microscopic examination of the eye*—discoid tumor near optic nerve; adenocarcinoma of the choroid; cylindrical epithelium. *Remarks*—patient in "good health;" had rapid loss of vision; diagnosis intraocular growth; enucleation; patient became rapidly cachectic; was seized by violent pain in the head, and expired very suddenly. Gayet published this as a case of adenoma of the choroid, but it is obvious that this was a metastatic carcinoma of the choroid.

Case 10.—A. E. EWING[10] (St. Louis, Mo.). Female, aged thirty-two years. Primary growth; carcinoma of left breast the size of an apple; refused operation. Emaciated. Right eye first affected, then the left eye. O. D. vision lost in two months; O. S. vision sank to 20/200 in two or three weeks. O. D., small red tumor in anterior chamber attached to iris, extending to the ciliary body; anterior chamber shallow; detachment of retina; aqueous clear; O. S., extensive detachment of retina below. O. D. T. + 1. O. S. T. + 1 O. D. enucleated. *Duration of life*—about one year after first eye symptoms and enucleation. *Anatomical and microscopic examination of the eye*—discoid tumor lining choroid, surrounding the nerve, extending to the ciliary body on the temporal side; periphery of tumor thin; invasion of iris and ciliary body; diameter of growth 30 mm.; central elevation 1.5 mm.; carcinoma simplex. *Remarks*—O. D. wound healed kindly after enucleation; one month later vision began to fall in O. S.; tumor was now discovered in the breast. She was seen again six weeks after this, and had extensive detachment of retina. Health failed rapidly after enucleation, and Dr. Ewing expressed surprise that she could live with such extensive metastases. Yet Professor Voelkers writes to Dr. Ewing that she survived for about a year. She developed abdominal tumors and carcinoma of the liver. (Personal correspondence.)

Case 11.—O. F. WADSWORTH[11] (Boston). Female, aged forty-six years. Carcinoma of right breast amputated sixteen months before. Good health. Right eye affected. Vision lost in one month. *Ophthalmoscope*—macular tumor; sharply defined edge; light color; highest in the centre; retina detached below. Enucleation. *Duration of life*—a year or more after first eye symptoms and enucleation. *Anatomical and microscopic examination of the eye*—to the temporal side of nerve a discoid growth; medullary carcinoma; diameter, 12 mm.; height in centre, 3 mm.; rounded edges. *Remarks*—Dr. Wadsworth lost sight of the patient; believes she lived a year or more after enucleation. (Personal correspondence). For diagnostic purposes, aided by the ophthalmoscope, Dr. Wadsworth passed cataract needle into eye and pressed against tumor, which was hard and resisting. Eye was enucleated at patient's request.

Case 12.—S. SCHULTZ[12] (Frankfort-on-Oder). Female, aged thirty-four years. Carcinoma of right breast for one year. Left eye affected. Externally eye appeared normal; detachment of retina above and on temporal side. T. N. Enucleation. *Duration of life*—thirty-eight days after enucleation and four months and one week after first eye symptoms. Cause of death, bulbar paralysis. *Anatomical and microscopic examination of the eye*—two deposits, one above

the optic nerve on the temporal side, another below the nerve; first was 19 mm. broad by 5 mm. high; second was 5 mm. broad and 2 mm. high; medullary carcinoma; commencing perforation of sclera posteriorly. *Remarks*—had pain around eye with minus tension; pain followed the distribution of trigeminus.

Case 13.—A. ELSCHNIG[13] (Graz). Female, aged fifty-seven years. Carcinoma of left breast removed ten months before. Left eye affected. Very rapid loss of vision. Externally the eye appeared normal. *Ophthalmoscope*—retina detached above and below the nerve; became complete in a short time; fovea, dark red color; later the eye presented a glaucomatous appearance. T. +; painful. No operation. *Duration of life*—fifteen weeks after first eye symptoms. Cause of death, carcinomatosis. *Autopsy*—metastases in brain, lungs, and liver. *Anatomical and microscopic examination of the eye*—discoid tumor surrounding the nerve, principally on the temporal side; scirrhous carcinoma; choroid infiltrated and about twice normal thickness for 13 mm. around nerve; carcinomatous cells found in bloodvessels; retrograde metamorphoses in older portions of growth; iris adherent to cornea at filtration angle. *Remarks*—had paralysis of left recurrent laryngeal nerve; became comatose before death.

Case 14.—UHTOFF[14] (Berlin) (second case). Female, aged forty-seven years. Carcinoma of right breast amputated nine months before. Left eye first affected, then right eye. Very rapid loss of vision. *Ophthalmoscope*—grayish-yellow elevation; whitish spots; O. D. height + 7 D.; O. S. height + 9 D. No operation. *Duration of life*—six weeks after first eye symptoms. Cause of death, carcinomatosis. *Autopsy*—metastases in right temporal lobe, liver, spleen, kidney, bronchial and retroperitoneal glands, lung, and right suprarenal. *Anatomical and microscopic examination of the eye*—shell-shaped deposits posteriorly on temporal side; scirrhous carcinoma; large spaces full of necrotic tissue, in which cells can be outlined by careful focusing; retrobulbar perforations of the sclera. *Remarks*—died forty-four days after entering the hospital; was insane; became totally blind before death.

Case 15.—W. A. HOLDEN[15] (New York). *Anatomical and microscopic examination of the eye*—three separate deposits on temporal side; discoid tumor; diameter, 12 mm.; thickness, 1.5 mm.; small episcleral deposit at same point, but not connected; slight infiltration of choroid 4 mm. to the nasal side of the optic nerve; retina detached from papilla to ora serrata on the temporal side; cells in the capillaries and in the large veins of the choroid. *Remarks*—clinical history of case was lost.

Case 16.—S. SCHULTZ[16] (second case). Female, aged thirty-nine years. Carcinoma of right lung of six months' duration. Cachectic. Left eye affected. Vision lost in six weeks. Externally the eye appeared normal; behind the pupil could only see a vascular membrane, the detached retina. Very painful. Enucleation. *Duration of life*—four months after enucleation and seven months after first eye symptoms. Cause of death, marasmus. No autopsy. *Anatomical and microscopic examination of the eye*—discoid tumor on temporal side of the nerve; extra-scleral growth posteriorly; tumors, diameter 20 mm., height 3 mm.; extra-scleral growth 6 mm. by 4 mm.; connected by perforation of sclera; found a posterior ciliary artery plugged with epithelial cells; scirrhous carcinoma; hemorrhages in cell nests; no cells found in bloodvessels of choroid, but they were found in scleral bloodvessels; pigment in choroidal stroma; no pigment in scleral stroma. *Remarks*—the observations regarding the pigment found in these tumors is of value as showing that it is only the normal pigment of the choroid and retina which has been distributed by the growth, and that no reason exists for calling them "melanotic carcinomas."

Case 17.—V. KAMOCKI[17] (Warsaw). Male, aged thirty-seven years. Malignancy was not suspected. Best of health. Right eye affected. Vision was lost when first seen. Externally the eye appeared glaucomatous; detached retina closely applied to posterior surface of lens; much darker than usual; no wavy motion. T. +; very painful. Enucleation. *Duration of life*—a few weeks after enucleation and one year after first eye symptoms. Died suddenly soon after enucleation. No autopsy. *Anatomical and microscopic examination of the eye*—flat nodular tumor surrounding the optic nerve; diameter, 18 mm.; height, 5 mm.; sharply defined from healthy choroid; nerve invaded; adenocarcinoma; areas of colloid degeneration. *Remarks*—Kamocki had no suspicion of carcinoma, as the patient appeared to be in perfect health; diagnosis was adenoma of the choroid from lacrymal gland structure, congenitally included in the eye; diagnosis was changed when it was learned that the patient died very suddenly a few weeks later, probably from cerebral metastases; very similar to Gayet's case.

Case 18.—H. D. NOYES[18] (New York). Female, aged fifty-five years. Carcinoma of breast removed fifteen years before. Right eye affected. *Ophthalmoscope*—small elevation in macula of + 4 D.; color darker than the surroundings. T. —; pain. Enucleation. *Anatomical and microscopic examination of the eye*—carcinoma simplex; height of tumor, 1.5 mm. *Remarks*—began by rapid increase of hypermetropia from May to June of + 1.5 D. In August first ophthalmoscopic change was seen. I have been unable to secure any further information regarding this case than is to be found in Dr. Noyes' report.

Case 19.—G. ABELSDORF[19] (Berlin). Female, aged forty-four years. Carcinoma of right breast for one year. Left and right eyes simultaneously affected; left more advanced. In three weeks vision reduced to counting fingers. *Ophthalmoscope*—O. D. retina detached over macula; O. S., extensive detachment of temporal side. O. D. T. N.; O. S. T. N. *Duration of life*—three months and three weeks after first eye symptoms. *Anatomical and microscopic examination of the eye*—O. D. and O. S. nearly entire choroid invaded to ora serrata; choroidal deposits 2.5 mm. thick; sharp periphery; scirrhous carcinoma; deposits in iris, ciliary body, optic nerve, and sclera; emboli of epithelial cells in post-ciliary arteries; carcinomatous cells in blood-vessels.

Case 20.—G. H. MATTHEWSON[20] (Montreal). Female, aged forty-eight years. Primary growth. Carcinoma of thyroid. Right eye affected. *Ophthalmoscope*—small, flat, ovoid swelling below nerve; retina detached beneath growth. Posterior sclerotomy for amotio retinæ. Enucleation. *Anatomical and microscopic examination of the eye*—flat, rough tumor below nerve; adenocarcinoma; invasion of optic nerve and sclera. *Remarks*—sclera was punctured for detachment of retina, but fluid re-formed in twenty-four hours; eye was enucleated three months after first eye symptoms; patient was living when case was reported.

Case 21.—C. DEVEREUX MARSHALL[21] (London). Female, aged fifty-seven years. Scirrhous carcinoma of right breast of seventeen months' duration. Right eye affected. Vision lost in two months. Patient not seen by author. T. N. Enucleation. *Duration of life*—three months after enucleation and five months after first eye symptoms. Cause of death, abdominal metastases. *Anatomical and microscopic examination of the eye*—discoid tumor posteriorly; medullary carcinoma; periphery of growth split choroid like a wedge; optic nerve invaded.

Case 22.—C. DEVEREUX MARSHALL[21] (second case) (London). Female, aged forty-four years. Breast amputated eighteen months before. Very feeble. Right eye first affected, then left eye. Vision lost in few weeks. O. D.; pupil sluggish. *Ophthalmoscope*—fundus unevenly hypermetropic; gray elevation around nerve; optic nerve lies in depression; veins large, but not tortuous; O. S. appearance same as in right above disk. No pain; O. D. T. N.; O. S. T. N. *Duration of life*—seven or eight months after first eye symptoms. Cause of death, exhaustion. *Remarks*—clinical diagnosis only; the history and course of the disease was typical of carcinoma of the choroid.

Case 23.—KAEMMERER[22] (Erfurt). Female, aged fifty-eight years. Primary growth. Carcinoma of liver. (?) Very cachectic. Right eye affected. Vision lost in a few weeks. O. D.; mydriasis; no pupil reflex to light; blepharitis; corneal opacity; no external inflammation; highly myopic. *Ophthalmoscope*—old choroiditis; optic nerve covered by bluish-white detachment of retina; O. S.; myopia; choroiditis; staphyloma cornea. *Duration of life*—short time after first eye symptoms. Cause of death, exhaustion. *Autopsy*—"diffuse" carcinoma of liver; no nodules; liver contracted; no stroma found microscopically. *Anatomical and microscopic examination of the eye*—O. D.; flat nodular tumor posteriorly, one-quarter area of eye; yellow-gray color; 3 mm. high in centre; some nodules 7 mm. high; sclera invaded; no alveolar structure demonstrable, but found network of elastic fibres; large polygonal cells. *Remarks*—the author found no alveolar structure either in the primary liver growth or in the choroid, and speaks of all deposits as being infiltrations. Carcinoma without any stroma is, however, a difficult diagnosis to digest. The author argues that this carcinomatous infiltration of the liver is evidence of a carcinomatous germ infection. As all the deposits discovered were infiltrations, it raises a suspicion that they were metastases, and that the primary growth was not located.

Case 24.—WAGENMAN.[23] Female, aged forty-five years. Carcinoma of breast removed one year before. Good health. Right eye first affected, then left eye. Vision reduced to fingers in three weeks. *Ophthalmoscope*—O. D.; tense gray detachment of retina around papilla; height of detachment + 5 D.; O. S.; flat, grayish-white elevation in macula. *Operation*—O. D. enucleated. *Duration of life*—four months after enucleation and five months after first eye symptoms. Cause of death, carcinomatosis. No autopsy. *Anatomical and microscopic examination of the eye*—O. D.; discoid tumor on temporal side and surrounding nerve; sharp demarcation from surrounding fundus diameter, 20 mm.; height, 1 mm.; carcinoma simplex; sclera invaded near vena vorticosa; O. S. not examined. *Remarks*—O. D.; eye trouble commenced with a "glimmering;" O. S.; one month after enucleation of right eye the same "glimmering" appeared in the left eye; became totally blind before death; husband was syphilitic.

Case 25.—FELIX LA GRANGE.[24] Female, aged forty-eight years. Carcinoma of breast removed two years before. Right eye affected. Total detachment of retina; tumor in iris. T. + 1; pain. Enucleation. *Duration of life*—two months after first eye symptoms. Cause of death, carcinomatosis. *Anatomical and microscopic examination of the eye*—flat, shell-shaped growth on temporal side of nerve; carcinoma simplex; retina perforated by growth; deposits in iris and sclera; carcinomatous cells in bloodvessels.

Case 26.—JOHN ROWAN.[25] Male, aged fifty-five years. Primary growth. Carcinoma of lung; pain in lung for four months. Cachectic. Left eye affected. *Ophthalmoscope*—O. D.; glaucomatous cupping of disk. O. S.; immobile detachment of retina posteriorly and below. O. D. T. N.; O. S. T. N. *Duration of life*—four and one-half months after first eye symptoms. Died suddenly. *Autopsy*—carcinoma of lung. *Anatomical and microscopic examination of the eye*—discoid tumor of choroid posteriorly; central elevation 4 mm.; scirrhous carcinoma; detached retina extensively invaded. *Remarks*—enlarged cervical glands.

Case 27.—DE SCHWEINITZ[26] and STEELE. Female, aged forty years. Carcinoma of breast amputated six months before. Right eye affected. *Ophthalmoscope*—media clear; flat, broad, grayish-yellow thickening in macular region; edges of infiltration thin; central elevation + 6 D.; periphery level with fundus. T. N. Eye was enucleated. *Duration of life*—thirteen weeks after enucleation and sixteen weeks after first eye symptoms. Cause of death, brain metastases. *Anatomical and microscopic examination of the eye*—carcinoma simplex; size of growth, 14 mm. broad, 2 mm. thick; very large alveoli with necrotic foci; vessels plugged by carcinomatous cells. *Remarks*—recurrence of growth in breast, clavicular, cervical, and axillary glands.

Case 28.—CH. BENTZON.[27] Male, aged thirty years. Primary growth. Carcinoma of a dermoid cyst in right suprarenal body. Right eye affected. Vision lost in two months. When first seen it was supposed to be choroiditis centralis extending from macula to the disk; later an extensive detachment of retina occurred. Early intermittent attacks of pain. *Duration of life*—seven months after first eye symptoms. Cause of death, carcinomatosis. *Autopsy*—carcinoma of right suprarenal, right and left lungs, and mediastinal glands. *Anatomical and microscopic examination of the eye*—greenish-white mass, involving entire O. D.; posterior half of eye was lost; choroid and ciliary body replaced by papillary adenocarcinoma with very large acini. *Remarks*—father died from carcinoma of the rectum. The history indicates that glaucoma developed. First symptom was central scotoma. Became blind in eight weeks.

Case 29.—W. C. ROCKLIFFE.[28] Female, aged forty-six years. Primary growth. Scirrhous carcinoma of the breast. Left eye first affected, then the right eye. In one month vision in O. S. was reduced to fingers. *Ophthalmoscope*—O. S.; four cyst-like retinal detachments below the disk, bulging into vitreous; optic neuritis; hemorrhages into disk. O. S. T. + ;? severe pain; O. D. T. N. O. S. enucleated. *Duration of life*—' wenty weeks after enucleation and about nine months after first eye symptoms. C death, carcinomatosis. *Anatomical and microscopic examination of the eye*—O. S.; flat tumor, extending from nerve to ciliary process; height at nerve, 2 mm.; the growth split the choroid, which covered it on each side; scirrhous carcinoma; optic nerve and sclera invaded. *Remarks*—pain with a doubtful tension. Papillitis was marked, and detachment occurred close to the nerve before deposits could be seen with the ophthalmoscope. This history suggests a possible invasion *via* the arteria centralis retinæ.

Case 30.—E. L. OATMAN (Brooklyn, N. Y.). Male, aged fifty-six years. Primary growth. Carcinoma of liver. Apparently in good health. Left eye affected. Vision lost in six weeks. When first seen the eye had become glaucomatous; posterior synechia; gray, non-vascular, smooth mass closely applied to posterior surface of lens. T. + 1; very painful. Enucleation. *Duration of life*—thirty-five days after enucleation and eighteen months after first eye symptoms. Cause of death, carcinomatosis; pneumonia. *Autopsy*—metastases in right lung and right bronchus, right suprarenal, right and left kidneys, spleen, bronchial and retroperitoneal glands; falx cerebri; tentorium cerebelli pia mater. *Anatomical and microscopic examination of the eye*—papillary cyst; adenocarcinoma. (See text.) Remarks—(see text).

Decision as to the apocryphal character of the following cases must be left to the judgment of the reader.

I more than suspect that the following case was one of metastatic carcinoma of the choroid, although not so considered by the author.

Reported by Ch. Guende.[29] Female, aged fifty-four years. Tumor of right breast, supposed by Guende to be carcinoma, although a fragment removed for microscopic examination did not yield satisfactory results. She was very cachectic. Had four "nut-sized" bony growths on the skull. Many painful nodules on the sternum. Vision of O. D. had been failing for nine months. Six months before coming under observation she received a blow in this eye from an umbrella, which

excited violent reaction. Recurring attacks of cyclitis followed. Tension was minus, but pain was intolerable. With the ophthalmoscope he saw a yellowish-gray tumor, with scattered pigment spots, 2 mm. high, its border fading into the surrounding fundus. The retina was detached below the growth. This describes a carcinoma. It is very curious that in Schapringer's[8] case (Case 6), which was unquestionably carcinoma, there was a bony tumor on the skull one and one-half inches above the right ear.*

Guende followed the case no further, but ventures a diagnosis so remarkable that no efforts should have been spared to confirm it, namely, that this patient had carcinoma of the breast, and coincidently a sarcoma of the choroid.

Carl Wagner.[30] Male, aged forty-five years. Tumor of liver and stomach. Had been blind in left eye for eighteen months. Eye became glaucomatous; with the ophthalmoscope a "pea-sized" tumor was seen on the *nasal side at the equator*. Died soon after enucleation. Eye symptoms had existed for two years before death. The choroidal tumor was 2 mm. high, and was diagnosed by the author, who examined it microscopically, as a carcinoma. Metastases were found in the stomach, liver, and in the glands of the axilla, neck, and groin.

The long duration of the eye symptoms is suspicious. In no other case which has ever been reported was a carcinomatous metastasis deposited in the choroid as far forward as the equator. The other metastases suggest primary sarcoma of the eye. We have in addition the positive statement of S. Schultz,[16] who examined a section of this tumor, that it was a large round-cell sarcoma.

Samelsohn[31] briefly mentions a case which he considers to be metastatic carcinoma of the choroid, and promises a full report of the case later. Patient was a woman with carcinoma of the breast and pleura. Difficulty of vision had existed for two years. She had an intraocular tumor which had extended to the orbit. I have omitted this case without intending to question the well-known accuracy of the author's powers of observation, but simply because the preliminary report is so incomplete that no opinion can be based upon it. Possibly in a later paper, which has escaped my notice, he has verified the diagnosis.

Schoebl,[32] in his masterly contribution, "Diseases of the Retina," describes two cases of carcinoma of the choroid. The first is probably Case 7 of my table, reported by Mitvalski.[5] The second case is open to discussion. In 1881 Schoebl found a pigmented tumor of the cornea. Two years later he discovered a choroidal deposit surrounding the nerve. His clinical diagnosis was sarcoma, but the microscopic examination of the corneal growths showed a stroma containing epithelial

* Probably growing along the squamous suture.

cells, and the diagnosis of carcinoma was based on this. Schoebl very justly pronounces this case unique. My reasons for questioning this conclusion, aside from the age of the patient and the pigmentation of the growth, is the fact that it originated in and was confined to the connective tissue elements of the cornea, namely, the substantia propria. Schoebl emphasized the fact that Bowman's and Descemet's membranes were not involved. Modern pathology does not permit carcinoma to originate in connective tissue. Alveolar sarcoma or endothelioma would probably be a safer diagnosis. Whatever its histological character, it was a case of extreme interest.

This leaves thirty cases which may be accepted as probably genuine. In twenty-six a microscopic examination confirmed the diagnosis. The ages of the patients range from thirty to fifty-eight years, the average being 44.37 years. Twenty of the primary growths were situated in the breast, three in the lungs, two in the liver, one in the stomach and liver, one in the thyroid, and one in a dermoid cyst of the suprarenal body. In two cases—Holden's[36] and Kamocki's[17]—carcinoma not being suspected until after the histological examination of the eye, the patients passed from under observation, and the primary growth was not located. Twenty-two of the cases were females and seven were males. Although we have three females to one male affected, I am inclined to believe that this is not so much due to influence of sex as to the greater frequency of carcinoma of the breast in women, our statistics showing that the majority of eye metastases originated in carcinoma of the breast. It is of interest to note that in one male[5] (Case 8) the primary growth was in the breast. In every case so far reported the deposit commenced in the posterior portion of the choroid over the point of entrance and distribution of some one of the short ciliary arteries. The exact location is described as on the temporal side of the nerve in eighteen cases, above the nerve in one case, below the nerve in one, and around the nerve in two.

In all stages of carcinoma the cells exhibit a marked preference for the lymph channels as a route of emigration. Yet when the disease is far advanced the bloodvessels also are undoubtedly employed for this purpose. As we know of no lymph currents that could convey the cells from an abdominal or thoracic carcinoma to the eye, it may be assumed that they are brought hither by the vascular system. Consequently we can understand why the macular region of the eye would be the destination of am embolus seeking the easiest and most direct route from the heart to the choroid, namely, by way of the common carotid artery, and subsequently leaving the ophthalmic artery by one of the branches which enter the temporal side of the globe.

I am unaware of any case in which malignant disease has invaded the eye by way of the arteria centralis retinæ. Dittrich,[33] Krahm,[34]

Elschnig,[35] and Holden[36] have reported cases of metastatic carcinomatous deposits in the optic nerve. In every case, however, the neoplasms were located in the neural sheaths and infiltrated between the fasciculi of the nerves. The central vessels were filled with blood or occluded by a contiguous extension of the growths, the primary route of invasion being from the brain outward along the lymph channels.

An analysis of the early cases led observers to the conclusion that the left eye was more frequently invaded than the right, for the reason that a cardiac embolus enters by preference the left common carotid artery. Our table, however, tends to disprove this theory, as it shows that twenty right eyes and nineteen left eyes were attacked. Holden[15] (Case 15) does not state in which eye the deposit occurred. Both eyes were involved in ten, or one-third of all the cases.

No satisfactory explanation has as yet been offered of the fact that when this extremely rare metastasis occurs in one eye the other eye is peculiarly liable to a similar invasion.

Ten of the thirty cases here tabulated were bilateral.* Had the duration of life been longer in these cases it is reasonable to suppose that this percentage would be much higher. The theory of Manz and Wagner, that the cells travel from one eye to the other along the lymph channels of the optic nerves, is untenable, for, as Schultz[16] points out, if this were true, the metastasis would develop in the papilla—a condition which has never been observed. On the contrary, the site of its appearance in the second eye is analogous to that in the first, namely, at the point where a short ciliary artery enters the eye. In two of our cases —Ewing's[10] and Wagenman's[23]—the disease made its appearance in the second eye a month after the first had been removed.

Carcinoma is at present a subject of the most active investigation, and it is possible that we may be forced to modify our present views regarding its etiology and methods of systemic dissemination. Whatever the materies morbi may be—lawless cells or protozoa—we may assume from the wide distribution of secondary deposits that, in its advanced stage, it invades the entire system of its victim, subjecting all parts to its influence; yet the unknown factor which determines the location of a secondary deposit spares the organ of vision in all but the rarest cases. If the choroid owes its usual exemption from secondary carcinomatous deposits to the anatomical fact that it is a remote and inaccessible region, and that a carcinomatous embolus reaches it only rarely and by chance, then why, when it occurs in one eye, should the second eye, which is equally remote and inaccessible, be subjected to the same rare accident in one-third of all cases? It is difficult to understand why an unusual accident occurring to one eye should predispose its fellow to the same misfortune. The only explanation that offers itself to my mind is

* Holden's case[15] is necessarily omitted because it has no clinical history.

the assumption that the choroids are usually protected from the development of secondary carcinomatous deposits by conditions other than mere anatomical inaccessibility, and that when such a deposit does occur it is not due to chance, but rather to the fact that the unknown conditions which nearly always prevent infection are now suspended and fail to afford protection, thus leaving not only one but both choroids vulnerable and in a favorable condition for the growth of the carcinomatous processes. *A priori*, both are affected in one-third of all the cases.*

The shape and method of growth of these tumors is very characteristic. The almost universal type is a flat, disk-shaped thickening of the choroid, highest in its centre, which is usually in the macular region and sloping off to a thin-edged periphery. The tendency is to spread laterally, thus differing from sarcoma, which grows forward into the vitreous, forming a protuberant mass.†

As carcinoma and sarcoma possess no inherent tendency to this difference in form, the occurrence of such morphological variations in the eye can be best explained by assuming that it is due to environment. Sarcoma is primary in the choroid, originating in the walls of its blood-vessels. It is a growth of the fixed tissues of the eye, circumscribed, and of comparatively slow development. It naturally meets with the least mechanical resistance to its growth by pushing out into the vitreous.

As the choroid possesses no epithelial structures from which a carcinoma could develop, its presence here is always metastatic. It is in the nature of an infiltration by foreign elements, namely, epithelial cells, into the sponge-like lymph spaces of the lamina suprachoroidea, and along the perivascular and other lymph channels.‡

These cells naturally follow the path of least resistance, namely, laterally from the original foci. In rare instances a rapidly growing carcinoma in an advanced stage may reach a considerable height, as in Hirschberg's case,[6] where the elevation was 9 mm. This, however, was found post-mortem, and has no clinical significance.

Although the development of a choroidal carcinoma is much more rapid than a sarcoma, yet, judging from the reports, a small carcino-

* It is worth noting that in Uhtoff's case both ovaries and both cerebral hemispheres were affected. In Bentzon's case both lungs, and in my case both kidneys.

† The rare spindle-cell sarcoma of the choroid is usually a sessile tumor. I have never seen one assume the disk shape common in carcinoma. The only exception to this form is a case of sarcoma mentioned by Griffith[37] (case of Dr. Little), in which the growth assumed a "cake-like" form similar to carcinoma. Griffith ventures the opinion that had it been possible to obtain an ophthalmoscopic view the diagnosis of sarcoma would not have been made. Although I have no intention of questioning the diagnosis in this case, I have seen a case of chronic inflammatory thickening of the choroid assume exactly this form and organize into a cellular structure so closely resembling sarcoma microscopically as to deceive far abler observers than myself.

‡ Although cells have been found in the capillaries, the principal development of carcinoma is not in the lumen of bloodvessels but in lymph spaces.

matous deposit produces far more extensive detachment of the retina than does a central sarcoma of equal size. The explanation for this may be found in the different histological structures of the two growths, a sarcoma, as we know, being a connective tissue formation, while the cells of a carcinoma of the choroid are always of the glandular epithelial type, possessing an abortive function whose perverted secretion may assist in detaching the retina. Griffith[37] calls attention to the fact that central sarcomas in their early stages are often unattended by any subretinal effusion; but this does not hold true of sarcomas situated near the equator, which naturally interfere with the large emissary veins. The writer's view is that the subretinal effusion which attends sarcoma of the choroid is in a measure produced mechanically by interference with the circulation, while in carcinoma the early effusion is in part at least an exudate from the tumor itself.*

In Case 34, by Rockliffe,[28] the patient, although under constant observation, had detachment of the retina before the deposit could be seen ophthalmoscopically.

The time from the first eye symptoms until vision is reduced to counting the fingers is measured by weeks instead of by months or years, as is the case in sarcoma. Schoeler[3] gives the time as one month; Mitvalski[5] (Schoebl[32]), two weeks; Ewing,[10] two or three weeks and two months; Wadsworth,[11] one month; Schultz,[16] six weeks; Abelsdorf,[19] three weeks; Marshall,[21] two months; Wagenman,[23] three weeks; Bentzon,[27] two months; Rockliffe,[28] four weeks; Oatman, six weeks. The others are less exact, but generally speak of the vision as being lost "very rapidly."

The tension of forty-one eyes is described as normal in sixteen, increased in eleven, diminished in three, and not recorded in eleven. In Case 7, Mitvalski,[5] the tension was at first normal; later it was slightly minus, but soon afterward it increased, and the eye became glaucomatous.

Devereux Marshall[38] has studied the question of tension in intraocular growths, and his conclusions, which are evidently sound, show that in sarcoma confined to the choroid alone the tension is increased in about two-thirds and normal in about one-third of the cases, but is rarely if ever decreased. In carcinoma, as is shown by the preceding abstracts, these figures are reversed, about one-third having increased and two-thirds normal or possibly diminished tension. Still I am inclined to believe that a carcinomatous eye would enter the glaucomatous stage as frequently as one affected with sarcoma were its progress not arrested by the early death of the patient.

* It is not the writer's intention to advocate any of the various opposing theories that more or less imperfectly attempt to account for all cases of amotio retinæ in intraocular tumors, but the disproportionately large detachment which attends carcinoma in its *early stages* requires explanation.

About the only conclusion to be drawn from these observations is that an intraocular growth limited to the choroid and with minus tension is not a sarcoma.*

Although much labor has been expended in the study of tension in intraocular growths, too much reliance should not be placed upon it in differential diagnosis, as its variations probably depend on conditions other than the histological structure of the growth.

There is great uniformity in the following descriptions of the ophthalmoscopic pictures of early carcinomatous deposits by those observers who have been so fortunate as to obtain an examination before detachment of the retina had obscured the view.

It must be borne in mind that these descriptions are by different observers of different cases.

Case 2, by Hirschberg.[2]—O. D. Small, round, yellowish deposits around the papilla; central elevation 1.5 mm., fading off into the surrounding normal fundus. O. S. presented the same picture; central elevation, 1 mm.

Case 3, by Schoeler[3] and Uhtoff.—O. D. Retina was detached, but a grayish-white ring could be distinguished encircling the nerve. O. S., grayish-white, pinhead sized deposits in the macular region. The refraction changed from — 1 D. to + 1 D. while under observation.

Case 6, by Schapringer.[8]—In the macular region a reddish-white discoloration, with scattered pigment. Central elevation + 3.5 D.; slight detachment below the growth; eighteen days later the elevation was + 4.5 D.

Case 7, by Mitvalski.[5]—Oval growth on temporal side of nerve, fading off into the surrounding fundus; dirty-yellow color, with scattered pigment.

* Marshall[39] also has a later paper on the same subject, which tends to confirm his previous conclusions. It is interesting in this connection to direct attention to a paper by Casey Wood[40] and Brown Pusey on primary sarcoma of the iris which rather tends to disprove Marshall's conclusions. Sixty-three cases are tabulated, in many of which the ciliary body was involved. The tension in twenty-five cases is mentioned as plus in thirteen, normal in eleven, and minus in one.

Devereux Marshall's[38] tables, compiled from cases more or less under his personal observation, are as follows:

Sarcoma of the choroid . . . . . 53 cases.
Tension was + in 36 = 67.72 per cent.
Tension was N in 16 = 30.18 per cent.
Tension was — in 1 = 1.88 per cent.

Marshall doubts the accuracy of observation in the single case with diminished tension.

Sarcoma of the iris and ciliary body . . . . . 28 cases.
Tension was + in 10 = 35.71 per cent.
Tension was N in 14 = .50 per cent.
Tension was — in 4 = 14.28 per cent.

Glioma of the retina . . . . . 19 cases.
Tension was + in 7 = 36.84 per cent.
Tension was N in 10 = 52.63 per cent.
Tension was — in 2 = 10.52 per cent.

Case 8, by Mitvalski.[5]—Flat, oval elevation in the macular region; central elevation, 1 mm.; dirty yellow color, with whitish patches and scattered pigment spots.

Case 11, by Wadsworth.[11]—Sharply-defined macular tumor, highest in the centre, and sloping to the periphery; light in color; retina detached below.

Case 15, by Uhtoff.[14]—O. D. Yellowish-gray elevation, with whitish spots; central elevation + 7 D. O. S. presented the same picture on the temporal side of the nerve. Central elevation was + 9 D.

Case 22, by H. D. Noyes.[18]—Hypermetropia increased to + 1.5 D. in one month; two months later H. = + 4 D., and a small elevation darker than its surroundings was seen in the macula.

Case 24, by G. H. Matthewson.[20]—Small, flat, ovoid swelling below nerve. Extensive detachment of the retina.

Case 26, by Marshall.[21]—Fundus elevated around the nerve; red reflex lost; nerve was not choked. No hemorrhages noticed.

Case 28, by Wagenman.[23]—O. D. Flat, grayish-white elevation under the detached retina in the macula region. O. S. Flat, grayish-white tumor in the macular region.

Case 32, by de Schweinitz.[26]—Broad, flat, greenish-yellow deposit in the macular region. Height in the centre + 6 D. Periphery level with the fundus.

Case 33, by Bentzon.[27]—When first seen was diagnosed as central choroiditis. Eight weeks later the retina was extensively detached.

Case 34, by Rockliffe.[28]—This case presented a picture different from all the others. There was optic neuritis, with hemorrhage into the nerve, and four cyst-like detachments bulging in the vitreous.* As the case was under continuous observation it appears that the retina was detached before the deposits were visible to ophthalmoscopic examination.

The prognosis is, of course, bad, and the duration of life but brief. The average time from the first eye symptoms to death, as estimated from twenty-four cases, was about six and one-half months. The greatest expectation of life cannot reach two years. The usual cause of death is general carcinomatosis.

The subject of diagnosis of an intraocular growth, attractive as it is, should not be discussed here, but only such points as may serve to differentiate carcinoma from other conditions, notably sarcoma. Although it would not appear impossible to recognize a carcinomatous deposit ophthalmoscopically without knowledge of a pre-existing growth elsewhere in the body, I believe it has never been done. Carcinoma of the choroid is always a secondary deposit. Whether a sarcoma in the eye is ever secondary remains unsettled.

A few cases have been reported as such, and belief in its occurrence is proclaimed by some of our best observers. Schultz[16] accepts Braem-

* Papillitis appears to have been unusually pronounced in this case. Invasion *via* the arteria centralis retinæ would be unique. We trust that this point was investigated in the examination.

ser's[41] case without microscopic evidence; de Schweinitz[42] reports a case of his own;* but none are free from criticism.

Fuchs,[43] however, states dogmatically that metastatic sarcoma of the choroid is unknown, although he does not deny that it can occur. He collects 259 recorded cases of sarcoma of the choroid, none of which was secondary. In one case the tumor had existed in a blind, atrophic eye for twenty years, the patient succumbing at last to a metastatic deposit in the heart. It should not be forgotten that a peripherally situated sarcoma may remain in the eye for a long time without attracting the attention of the patient. The conditions necessary to establish the diagnosis of a metastatic sarcoma of the choroid are *the development of sarcoma in an eye known to be previously healthy in a person with a pre-existing sarcoma.* These conditions, so far as the writer's information extends, remain unfulfilled.

Carcinoma always appears posteriorly, usually in the macular region. It is a flat and disk-shaped infiltration beneath the retina, and its periphery, in the early stages at least, is level with the surrounding fundus. A sarcoma may be flat when very young, but it grows slowly forward into the vitreous as a rounded protuberance. Carcinoma is described as having a dirty yellow or whitish color, with scattered pigment. Sarcoma ranges from yellow to brown or black. No observers have mentioned that the carcinomatous growth appeared vascular. The overlying retina is usually described as œdematous or slightly detached. Sarcomas, on the contrary, often appear quite vascular. Carcinoma appears later in life than sarcoma. In sarcoma confined to the choroid alone, the tension is not diminished. (Marshall).

The pain of sarcoma is due to increased tension. In carcinoma it may be severe, with normal or diminished tension. (Noyes,[18] Schultz,[16] Bentzon,[27] and Rockliffe.[28]) A positive central scotoma is the usual initial symptom, but a rapid increase of hypermetropia, without any marked ophthalmoscopic changes, may occur, as in Noyes' case. When Schoeler[3] exhibited his case before the Berlin Medical Society in 1882, Hirschberg and Schweigger doubted the diagnosis, because no difference could be observed in the level of the fundus. But Schoeler said, however, that the choroid was diffusely thickened, and that the refraction had changed from -1 D. to $+1$ D. while under his observation. Uhtoff examined the eye post-mortem and found a carcinomatous

* de Schweinitz's case, if rigidly construed, may be accepted as a secondary invasion of the choroid by sarcoma. A man died from primary mediastinal sarcoma twenty-four hours after coming under observation. Necropsy showed extensive sarcomatous invasion of the optic nerves and orbital contents sufficient to produce marked exophthalmos. Only the posterior halves of the eyes were examined microscopically. Small areas of deep choroidal infiltration, with sarcoma cells, were found on the nasal sides of the optic nerves. In this case the eyes appear to have been invaded more by a contiguous extension from the optic nerves or orbital deposits than by a metastasis as generally understood. It must also be remembered that an insignificant choroidal sarcoma may produce fatal metastases.

choroid. The clavicular or cervical glands may or may not be enlarged. As this is an inconstant symptom, evidently depending on deposits located elsewhere than in the eye, its diagnostic value is only confirmatory as suggesting a carcinomatous diathesis.

A central conglomerate tubercle of the choroid may occur without any external inflammation of the eye, and it may not always be possible to locate other tubercular foci. It also may occur in subjects past middle life, but it differs from carcinoma by its rounded, protuberant form, the presence of satellite tumors, and a tendency to soften and perforate the sclera. Increase of tension is very rare in tuberculoma.

Detachment of the choroid, miliary tuberculosis, and choroiditis posticum could hardly be confounded with carcinoma by trained observers.

It must be borne in mind that the physical condition of the patients may not suggest the presence of malignant disease. In seven of our tabulated cases their good health was especially mentioned, and in many of the others it may be inferred from their histories.

All treatment is, of course, unavailing. The almost universally accepted rule that an eye should be enucleated as soon as the diagnosis of carcinoma of the choroid is made may be questioned. The late Henry D. Noyes[18] advised against subjecting these doomed patients to the ordeal of an operation unless rendered necessary by pain. His reasons were to spare suffering in a case where an operation could not hope to prolong life.

If the eye is painful or has entered the glaucomatous stage its removal is not to be criticised; but when, as in many cases, there is no pain, it may safely be left undisturbed without risk of shortening the life of the patient. The speedy death which, with two exceptions, has followed enucleation raises the suspicion that the operation may in some inexplicable manner stimulate the other deposits to increased activity. A similar view is held by many surgeons in regard to sarcoma which has invaded the orbit, experience seeming to show that the fatal termination is precipitated by surgical interference. C. S. Bull[44] cites thirty-six cases of orbital sarcoma occurring among his private patients, in which the condition was aggravated and death apparently hastened by efforts to remove the growths. The following cases, which include all in which the eye has been removed for carcinoma of the choroid, certainly seem to indicate that enucleation should be postponed until increasing pain renders it imperative.

Case 7, by Mitvalski.[5]—Patient had been in good health since amputation of the breast, two years before. Died two months after enucleation, from metastasis in the brain and lungs.

Case 9, by Gayet.[9]—Patient was in good health when the eye was removed. Cachexia immediately developed, and death followed in a few weeks from cerebral metastases.

Case 10, by Ewing,[10] and Case 11, by Wadsworth,[11] appear to be exceptions to the rule, although neither surgeon had the patient under his observation very long after the operation. In reply to my inquiries Dr. Ewing kindly wrote Prof. Voelkers, at Kiel, for the subsequent history of his case, and the reply stated that she survived the operation about a year. Although this patient did not perish immediately after enucleation, her health rapidly deteriorated, and Dr. Ewing[10] expressed amazement that life remained in a being so cachectic. Dr. Wadsworth* was unable to add anything to the subsequent history of his case, as it passed into other hands, but he believes that she lived about a year after the enucleation.

Case 12, by Schultz.[12]—Patient died thirty-eight days after enucleation from bulbar paralysis.

Case 16, by Schultz.[16]—The physical condition was bad. The eye, becoming painful, was removed. Death followed in four months.

Case 17, by Kamocki.[17]—Male, aged thirty-seven years, was in the best of health. Eye deposit began one year before, and vision had been abolished four months previous to enucleation. Shortly after leaving the hospital, where he appeared to be perfectly healthy, he became ill, and died in a few weeks.

Case 21, by Marshall.[21]—Eye symptoms for two months preceding operation. Died two months later from abdominal carcinoma.

Case 24, by Wagenman.[23]—Patient was in good health, but died four months after operation from general carcinomatosis.

Case 25, by Le Grange.[24]—Died two months after enucleation from general carcinomatosis.

Case 27, by de Schweinitz.[26]—Survived the operation thirteen weeks, dying from cerebral metastasis.

Case 29, by Rockliffe.[28]—Patient lived twenty weeks after operation.

Case 30, by Oatman.—Patient was apparently in good health. Vision had been abolished eighteen months. Operation was immediately followed by a rapidly progressing marasmus, terminating fatally in five weeks.

Considering the history of these cases, it is not probable that when a metastasis has occurred in one eye its removal will tend to prevent a similar deposit in the other.

In the cases of Ewing[10] and Wagenman,[23] the remaining eye was attacked a month after the removal of its fellow.

Other Operative Procedures.

Case 5, Manz.[7]—Performed posterior sclerotomy to relieve the pain. A thin, yellow fluid escaped, but no relief followed.

Case 11, Wadsworth.[11]—For diagnostic purposes, aided by the ophthalmoscope, passed a cataract needle into the globe and pressed it against the tumor, which felt hard and resisting. He is probably mistaken in supposing that the rapid loss of vision which followed was in any way influenced by this procedure.

* Personal correspondence.

Case 20, G. H. Mathewson.[20]—Performed posterior sclerotomy to relieve the detachment of the retina. Twenty-four hours later the fluid had re-formed.

Résumé. A review of the literature yields thirty cases which are considered genuine.

The average age was 44.37 years.

Twenty of the primary growths were situated in the breast, three in the lungs, two in the liver, one in the stomach and liver, one in the thyroid, one in a dermoid cyst of the suprarenal body, and two not located.

There were twenty-two female and eleven male cases. This preponderance of three females to one male is not due to influence of sex, but to the greater frequency of carcinoma of the breast among women. One male case had carcinoma of the breast.

Twenty right eyes and nineteen left eyes were affected. This disproves the prevailing theory that the left eye is most frequently invaded.

Both eyes were involved in ten cases. While the deposit of a carcinomatous metastasis in the eye is an extremely rare event, when it occurs in one eye the other eye is also invaded in one-third of the cases. This bilateral peculiarity is ascribed to some unknown factor which ordinarily prevents the development of metastatic carcinoma in the choroids, but in these particular cases it is for some reason in abeyance.

The deposit always occurs posteriorly near the point where a short ciliary artery enters the globe. It appears in the corresponding region of the second eye when the latter is attacked. This indicates that the second eye is not invaded by way of the lymph channels of the optic nerve and chiasm.

The typical shape is a flat discoid thickening of the choroid with a central elevation of two or three millimetres, gradually sloping off to a thin periphery. It spreads laterally, because it is an infiltration of the choroidal lymph spaces with epithelial cells which naturally follow the path of least resistance. Sarcoma, on the contrary, is a growth of the fixed tissues.

The time from the first eye symptoms until vision is destroyed varies between two and eight weeks. The average is about five weeks. This rapid loss of vision is due to an early and extensive detachment of the retina. As choroidal carcinoma is always composed of glandular epithelial cells, it is assumed that their perverted secretion actively assists in producing the amotio retinæ.

Tension is increased in one-third and normal or diminished in two-thirds of the cases.

A typical ophthalmoscopic picture is "flat oval deposit or tumor on the temporal side of the nerve, involving the macula, with a central elevation of + 3 D., its edges gradually fading off into the surround-

ing fundus. Its color is a dirty-yellow, with scattered pigment spots." (Mitvalski's[5] case.)

The average duration of life after the first eye symptoms is six and one-half months.

In the differential diagnoses between carcinoma and sarcoma the following points are noted:

Carcinoma of the Choroid.	*Sarcoma of the Choroid.*
Always secondary.	"Secondary sarcoma of the choroid is unknown." (Fuchs.[43])
Has always occurred posteriorly. Usually on the temporal side of the nerve.	May occur at any point.
A flat discoid tumor or thickening of the choroid which spreads laterally.	It is a rounded protuberance growing out into the vitreous.
Has not been described as appearing vascular.	May appear vascular.
Early detachment of the retina.	Late detachment when centrally located. (Griffith.[37])
Destroys vision in a few weeks.	May exist for a long time with good vision.
May be very painful with T. N. or T.—.	Pain is due to T. +.
First symptom may be a rapid increase of hypermetropia without marked ophthalmoscopic changes.	Too circumscribed to produce this phenomenon.
T. may be diminished.	If confined to the choroid T. is never diminished. (Marshall.[38])

Pre-existing carcinoma will, of course, suggest the character of the eye deposit; but in seven cases the good health of the patients was a subject of comment. In five carcinoma was first disclosed by the microscope.

Enucleation is not advisable unless the eye is very painful or glaucomatous, since the histories appear to indicate that an increased activity in the cancerous processes and a speedy death may be ascribed to operation.

When a metastasis has occurred in one eye its removal does not prevent a similar deposit in its fellow.

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A REPORT OF CASES OF ANÆMIA, WITH OBSERVATIONS UPON THEIR SYMPTOMS AND MORPHOLOGY OF THE BLOOD.

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I DESIRE to report the following cases, which occurred during the past winter in my service at the Pennsylvania Hospital:

Severe Secondary Anæmia Due to Repeated Metrorrhagia. Lizzie R., aged thirty years, white, married, housewife, born in Russia. Father died from unknown cause; mother died in confinement; has one sister in good health; lost one brother in childhood.

Past History. Has been a healthy woman. Has one child, aged seven years. Ten weeks after the birth of this child an infected right ovary was removed. Menstruation since this operation has been regular. After the operation she never recovered her former color. The present illness began two weeks ago, with constant but rather scanty bleeding from the vagina. She has had slight nose-bleed, with pain in the abdomen, headache, dizziness, ringing in the ears, and slight cough. She states that she has become very pale during this time. Bowels are constipated.

Admitted to the Pennsylvania Hospital March 5, 1902 (hospital No. 4014).

Physical Examination. She is a well-nourished woman. Face seems puffy; pupils equally dilated. Face and skin pallid, not lemon-tinted; mucous membranes and nails practically colorless. The radial pulse quick, of fair volume, and very compressible. Tongue pale, moist, with rather thick, yellowish coat; no venous phenomena. The lungs are normal. Visible cardiac impulse in the fourth interspace, 10 cm. from mid-sternum. On auscultation, a soft, blowing, systolic murmur, best heard in the third interspace, and also present at the pulmonary cartilage. Abdomen round, globular; nowhere tender. Liver and spleen normal in size. Vaginal examination: Neither ovary is felt; the cervix is rather soft, the uterus slightly increased in size. A small amount of dark brown vaginal discharge is present. The urine: Specific gravity 1014; acid; contains neither albumin nor sugar, and no casts. The blood showed: Erythrocytes, 910,000; leucocytes, 5300; hæmoglobin, 17 per cent. The differential count showed: Polynuclears, 80 per cent.; small lymphocytes. 13.6 per cent.; transitionals and mononuclears, 2 per cent.; eosinophiles, 4 per cent.; unidentified cells, 4 per cent. The unidentified cells are polynuclears without granules, and pale staining nuclei. The corpuscles are unusually small; show no polychromatophilia; no megaloblasts found. Three normoblasts were found during the examination of several slides. The patient had a temperature on admission of 100.2° F., which rose to 102° F. the following day. During the next seven days it gradually fell to normal.

She was put upon peptomangan, ½ ounce four times a day, with Fowler's solution, 3 drops, and adrenal extract, 1 grain, three times a day. She was given a fluid diet and 4 ounces of gelatin, twice a day. Her improvement in a week's time was remarkable, the blood count rapidly rising—erythrocytes, 2,630,000; leucocytes, 4600; hæmoglobin, 35 per cent. During this stage the differential count showed a slight diminution in the polynuclear leucocytes, with an increase in the small lymphocytes. One week later the erythrocytes had risen to 3,392,000; leucocytes, 3800; hæmoglobin, 62 per cent. Since her admission to the hospital there has been no evidence whatever of uterine hemorrhage or bleeding from any other source. She complains mainly of headache, thirst, and vague abdominal pains. Discharged at her own request on the 22d of March.

This case shows the rapid and severe anæmia induced by repeated small hemorrhages. The woman, who was rather a plump specimen, appeared as white as alabaster. Blood examination did not show the leucocytosis which is common after losses of large amounts of blood.

During convalescence the number of lymphocytes and normoblasts was not disproportionate, as some observers have noted; nor was there marked change in the size or form of the red cells.

Severe Secondary Anæmia. Cause not Ascertained, followed by Relapse and Death. Adolph K., aged fifty-four years, white, married, born in Germany. Family history not important.

Previous History. Healthy man; no severe sickness in life, no venereal disease; used beer very moderately. Present illness began several months ago with increasing pallor and weakness, shortness of breath, and swelling of the feet. This pallor was preceded by a diarrhœa of several weeks' duration. He was admitted to the hospital on October 24th (hospital No. 2132).

Physical Examination. He is a large-boned, fairly well-nourished man. Rather waxy appearance on face and skin, not lemon-colored. Sclera pearly; mucous membranes and nails very pallid; no pigmentation of skin. Comparatively few teeth remain in either jaw; gums shrunken, not ulcerated. Lungs normal. Heart normal except hæmic murmur at apex. The abdomen negative, with the liver and spleen normal in size. Slight œdema present on the dorsum of the feet and over the tibia. Blood: Hæmoglobin, 25 per cent.; erythrocytes, 2,380,000; leucocytes, 6500; differential count 250: polynuclears, 76 per cent.; small lymphocytes, 16.8 per cent.; transitionals and large mononuclears, 5.4 per cent.; eosinophiles, 8 per cent. The urine was normal in color; negative on chemical and microscopic examination. Examination of the stools revealed no intestinal parasites or eggs. Examination of a test-meal showed: Hydrochloric acid, 2 per cent.; total acidity, 40 per cent.; no lactic acid; pepsin present.

He remained in the hospital fifty-eight days, with a rather rapidly increasing red count. Thus by October 29th the erythrocytes were 3,987,000, the leucocytes 8650, with hæmoglobin 43 per cent. At this time there was a decided increase in the small lymphocytes, which reached 22 per cent., while the polynuclears dropped to 64 per cent. This blood state was not constant, for before his discharge the mononuclears again dropped to 11.6 per cent., the polynuclears rising to 76 per cent. He was permitted to return to his home on November 20th, with an erythrocyte count of 4,443,750, and a hæmoglobin percentage of only 50.

The improvement in this case was extremely rapid. He gained in color and in strength under the use of Blaud's pills. His blood showed but moderate poikilocytosis, with no macrocytes, while microcytes and elongated forms were fairly numerous. No nucleated reds were found, nor was there adequate cause ever discovered for the intense anæmia. The diarrhœa which was present two months before admission may have been its basis, though there was no evidence of blood in his stools at any time during his stay in the hospital.

I learn as I write these notes that he was admitted within a few days to the wards of my colleague, Dr. Lewis, having had a relapse, which began about February. His blood count upon readmission was: Hæmoglobin, 17 per cent.; erythrocytes, 2,140,000; leucocytes, 8600. He was extremely weak. In a few days the hæmoglobin had dropped to 13 per cent., with erythrocytes to 1,836,000. The eyes, examined by Dr. Harlan, show fields very pale, bloodvessels pale, almost invisible,

but no hemorrhages. The patient was permitted to leave the hospital because of extreme homesickness, and I learn he died twenty-four hours later. The differential count in this case at this time showed a slight polynuclear excess—80 per cent.; no nucleated reds were found.

It is possible that this case may exemplify a severe type of secondary anæmia which rapidly became pernicious.

Secondary Anæmia Due to Cancer of the Stomach. Margaret H., white, aged fifty-six years, domestic; mother of two children; no obtainable family history. Was at work one week before admission. Three weeks before admission is said to have had trouble with her stomach for several days, compelling her to stop work. Admitted to the hospital February 1, 1902 (hospital No. 3603).

Physical Examination. A small, rather stocky woman, somewhat irrational. Very few teeth in either jaw; no ulceration of gums. Face and body rather lemon-yellow in color; the mucous membranes and nails colorless. Pulse small, rapid, compressible. One or two small, bluish discolorations upon the arm; no evidence of hemorrhage elsewhere either in the mucous membranes or the skin. Lungs normal. Heart: systolic apical murmur. Abdomen soft; no mass palpable; winces somewhat on palpation in the epigastric region. No enlarged superficial lymphatic glands. Urine light yellow; contains no albumin or sugar. Blood: Hæmoglobin, 20 per cent.; erythrocytes, 1,000,000; leucocytes, 18,000. Differential count: Decided polynuclear excess, 90 per cent.; moderate poikilocytosis present; numerous nucleated reds; 125 seen in counting 50,000 leucocytes, mostly normoblasts.

In twenty-four hours the patient was decidedly worse; semiconscious; had vomited material, which, unfortunately, was not seen by the resident. Pulse imperceptible, though the heart continued to beat for twenty-four hours longer. Died February 4th. Autopsy showed a small colloid cancer, about 8 cm. in diameter, infiltrating the posterior wall of the stomach near the lesser curvature. There was slight involvement of the lymphatic glands behind the stomach and the head of the pancreas.

This case shows how numerous nucleated red cells may become in the peripheral blood in secondary anæmia. Had this woman been conscious, and had an examination of the gastric contents been feasible, the diagnosis of carcinoma would have been made with some certainty. In pernicious anæmia a terminal leucocytosis is common. The fact, however, that the majority of nucleated cells were normoblasts is an important factor in the diagnosis between the secondary anæmia due to cancer and pernicious anæmia. The cancer here was small and quite recent, and was probably not entirely responsible for the very severe grade of anæmia present in this case; in fact, these cases at times show the typical blood picture of pernicious anæmia.

Chlorosis, with Frequent Relapse and Obstinate Cardiac Symptoms. Maggie M., aged nineteen years, white, single, born in Ireland. Family history good, though one sister is said to be anæmic.

Past History. Menstruated at sixteen years; came to the United States when seventeen. Since arrival here has menstruated but four times. One year ago spent nine weeks in the University Hospital, with illness similar to present one; discharged much improved. Present illness: Sick for six months with headache, pain in both ovarian regions, weakness and shortness of breath on exertion. She has become very pale, and complains of pain in the eyes, left side of the face, in the abdomen, and left arm. Is very nervous, with poor appetite; has a decided fondness for candy and tea. Admitted to the hospital February 9th (hospital No. 3669).

Physical Examination. Rather buxom but pallid Irish girl. Mucous membranes pale; tongue coated; pulse regular, rather full and bounding. Lungs normal. Heart overacts, with loud, booming first sound and systolic murmur at the base. Increase in size of the left side. Liver and spleen normal in size. Abdomen soft and flat; no gastroptosis. Vaginal examination reveals an unusually small, infantile uterus. Pelvis negative. Urine light yellow, acid; specific gravity, 1027; no albumin, no sugar; calcium oxalate. Blood: Hæmoglobin, 38 per cent.; erythrocytes, 2,947,000; leucocytes, 7000; differential count: polynuclears, 71.5 per cent.; small lymphocytes, 18.5 per cent.; large mononuclears and transitionals, 7 per cent.; eosinophiles, 2 per cent.; mastzellen, 1 per cent. Blood cells are small and pale, with large central, non-staining portion. Moderate poikilocytosis; no polychromatophylia. Under forced diet, with large doses of Blaud's pills, combined with Fowler's solution and phosphate of soda as a purge, her blood condition improved slowly. On March 7th, hæmoglobin, 52 per cent.; erythrocytes, 4,279,000. On May 9th, hæmoglobin, 60 per cent.; erythrocytes 4,388,000. During all this time, however, the girl's heart would overact upon the slightest provocation. She complained constantly of smothering sensations about the heart, with palpitation. The use of purges to deplete the volume of blood; of local applications, such as the ice-bag over the heart; the use of bromides internally, seemed to be of no avail whatever, and she left the hospital with a greatly improved blood condition, although still complaining of vague pains and suffering with palpitation of the heart from the slightest cause.

This case presents a combination of causes, one of which seems alone able to produce chlorosis. Thus the disease is seen most frequently in girls about the menstrual developmental period; nostalgia is a frequent aid in its production. Dietetic errors—the abuse of tea, toast, and candy as habitual diet—are frequently met with. Its exact pathological basis is, however, difficult to find. Virchow's postulate—a hypoplasia of the heart, bloodvessels, and generative organs—will not hold, for many such conditions are found and no chlorosis exists. Hoffmann's and Sir Andrew Clark's view that absorption of toxins from the intestinal canal is the exciting cause does not cover all cases. It probably is to be found in the functional derangement in the hæmoglobin manufacturing process of the bone-marrow.

Lloyd Jones also believes that the total volume of plasma is much

increased in chlorosis. This will answer for the symptoms present in the above case—the palpitating, dilated heart, with throbbing vessels.

Acute Progressive Pernicious Anæmia; Death; Autopsy. Maggie J., aged thirty-two years, white, married, housewife by occupation; born in Philadelphia. Family history: Father died with asthma and mother of uterine hemorrhage; three brothers died in infancy, from unknown causes.

Past History. Measles in childhood; blindness of the right eye (phthisical ball). When fifteen years of age was severely burned over the back and chest and portion of the abdomen; was eight months in recovering. Has had seven children, five of whom are living, in good health. She states that before each child was born the skin became yellowish in color, and "the jaundice" disappeared after childbirth. Present illness began three months ago, a short time prior to the birth of her last child, which was born early in February, 1902. She complained of heartburn, with vomiting and constant eructation of gas, and a burning sensation in the mouth. Two weeks after the birth of her child (February 22d) she had a large hemorrhage from the bowel, which was repeated upon the subsequent day, though accompanied with less blood. For some weeks before admission she complained of sore gums. Her skin has been yellow for four months, and she states that "the jaundice" has been much deeper before admission than at the present time.

Admitted to the hospital March 18, 1902 (hospital No. 4181).

Physical Examination. She is a medium-sized, fairly well-nourished woman. Face and body are lemon-yellow color. Conjunctivæ distinctly yellowish. The tongue is moist, pallid, with smooth and glazed surface; breath is fetid. There are about six front teeth in the upper jaw, while the few remaining teeth are decayed. The lower jaw contains about seven front teeth; all the molars are missing. The gums on both the upper and lower maxilla are inflamed and suppurating; there are no hemorrhages of the mucous membrane. Chest: The lungs are clear both in front and behind. Heart of normal size, though with soft, hæmic systolic murmur at apex, and a similar but louder murmur at the pulmonic and aortic cartilages. The abdomen is round and very flaccid. There is a slight dark brownish pigmentation over the margins of a large scar, which extends from the middle of the back around to the front of the abdomen. No mass is felt in the abdomen; no glandular enlargement.

She remained in the hospital a little over four weeks. During the first two weeks there was considerable diarrhœa. On two occasions the stools contained a dark, gelatinous blood clot. Her temperature has been maintained between 100° and 101° F. The pulse soft, very compressible, averages 120. No evidence of dyspnœa. Rather sleepy mental condition, with disinclination to any exertion. Complains constantly of burning in her mouth and thirst. No pains over joints or bones. Cultures taken from the mouth showed large numbers of streptococci pyogenes. On March 30th the stomach contents showed no free hydrochloric acid, no lactic acid; total acidity of 14; combined hydrochloric acid 8, or 0.0288 per cent. The knee-jerks present on both sides increased; no ankle clonus. During the last two weeks of her life the patient developed a diffuse œdema of the back. The face

became puffy and the limbs œdematous. She complained of a constant ringing, of sounds, or music in her ears, and finally became totally deaf. There were no special cardiac or vascular symptoms. Left eye-ground, examined by Dr. Harlan, showed a high degree of astigmatic hypermetropia; disks white; whole fundus pale; venous blood scarcely darker than arterial; extensive retinal hemorrhage, striated and non-striated.

No parasite or eggs were discovered in her stools. Urine (April 13th): 1260 c.c. in twenty-four hours; specific gravity, 1009; reddish-yellow in color. Urea: 1.4 per cent. or 17.6 drachms in twenty-four hours; later examinations of urine showed lesser quantities of urea. No pathological urobilin was present; a large amount of indican was, however, found. Two quantitative estimates for indican gave 84 and 94 milligrammes for the twenty-four-hour specimen.

Blood: The day of admission the blood count was as follows: Hæmoglobin, 16 per cent.; erythrocytes, 744,000; leucocytes, 3700. A differential count showed: Polynuclears, 78.2 per cent.; small lymphocytes, 19.2 per cent.; large mononuclears and transitional cells, 1.2 per cent.; eosinophiles, 1.4 per cent. There was moderate poikilocytosis, with slight polychromasia. There were some megalocytes present; considerable endoglobular degeneration; two megaloblasts and two normoblasts were found. The red cells became fewer in number as time went on, notwithstanding food and medicine and the hypodermic administration of arsenic.

The erythrocytes slowly fell until, during the first week of April, the erythrocyte count was 268,000, with leucocytes 5900 and hæmoglobin 3 per cent. The coagulation time of the blood was six minutes; its specific gravity 1022. Blood cultures: All flasks remained sterile after five days. During the last week of life the woman seemed drowsy and complained but little. Skin dry; hair dry and lustreless; the ear held up to the light was bloodless, and resembled yellow parchment. Nails were bloodless. The condition of the gums was improved, and there was but slight odor to the breath. It was evident that she had lost flesh.

The last blood count was made two days before death. Erythrocytes, 393,000; hæmoglobin, 3 per cent. There was no terminal leucocytosis. The autopsy showed widespread fatty degeneration of the organs, especially the heart and liver. There were in the ileum, several feet above the ileocæcal valve, two scars, entirely healed, with slight pigmentation about them. They seemed to be Peyer's patches. There was no involvement of other parts. Spleen and liver of normal size. Bone-marrow dark red, not fatty.

Microscopic Examination. Large numbers of megalocytes and of nucleated erythrocytes, the majority of them megaloblasts; in many the nuclei are undergoing fragmentation. There are comparatively few leucocytes present. The polynuclear leucocytes are almost entirely absent, the majority of the leucocytes being myelocytes and lymphocytes; very few eosinophiles are present.

This case must, I think, be considered from both the clinical and pathological standpoint as one of pernicious anæmia—one of the cases, however, in which pregnancy seems to have been the exciting cause. The symptoms, however, coincide well with that group of cases to which

Hunter has recently called attention, namely, those with pyorrhœa and ulcerative gingivitis, with glazing of the tongue and gastro-intestinal symptoms. That the woman absorbed toxins from her intestinal canal is evident. She had great increase in her indican output, while there was no special evidence, excepting her hæmatogenous jaundice, in her urine or elsewhere, of great blood destruction. At first the blood examination showed but few megaloblasts and changes in size and shape. In the last two weeks of her life, however, nucleated cells became more abundant, chiefly megaloblasts, though the differential count at no time showed a disproportion of lymphocytes. Of five or six cases of pernicious anæmia seen during the last year, but one case presented this increase in lymphocytes, which is supposed to be characteristic of this disease. In this case I would call attention to the continuous high hæmoglobin index, 1.78 to 2 per cent. The rapid termination of this woman's life did not permit of the extensive changes in the morphology of the blood which are frequently observed in cases of much greater duration. The absence of polynuclear leucocytes in the bone-marrow and their apparent increase in the circulating blood is probably accounted for by the supposition that in such an acute process there is still some bone-marrow remaining unaffected which could manufacture polynuclear leucocytes. (I hope to report this case in greater detail in the future.)

Acute Lymphatic Leukæmia, with Death and Autopsy. Philip O. K., aged sixty-five years, white, married, painter by occupation. Family history of no interest.

Past History. No serious illness in life except numerous attacks of pain and swelling in the joints, called rheumatism. His wife and three or four grown-up healthy children living. Present illness began four days before admission, with headache, general body pains, high fever, and diarrhœa.

Admitted to the hospital November 14, 1901 (hospital No. 2672).

Physical Examination. Medium-sized, spare man, with dry, glazed tongue; teeth bad, majority lost; pyorrhœa. Chalky deposit in the ears, knuckles, elbows, and knees. Spleen much enlarged; rasping, systolic murmur at apex. Urine contains albumin; acid; specific gravity, 1012; on microscopic examination, hyaline, light and dark granular casts. Two days after admission constantly complained of hyperæsthesia of the entire body. No enlargement of the lymphatic glands. All parts of the skin subjected to pressure have become much reddened, with here and there minute punctate hemorrhages. Fever, which was high on admission, slightly reduced. Five days after admission right-sided pneumonia developed, with death in thirty-six hours.

The blood, examined day after admission: Erythrocytes, 2,731,250; leucocytes, 155,500; hæmoglobin, 60 per cent. On November 19th the leucocytes were 154,000; on the 20th, 205,780; and on the 21st, 283,000. Cultures from the circulating blood (November 21st) showed the presence of the micrococcus lanceolatus. Differential count on November 16th showed: Small mononuclears, 85.8 per cent.; polynuclears, 12 per cent.; large mononuclears, 1.6 per cent.; eosinophiles, 0.4 per

cent.; myelocytes, 0.2 per cent. Bacteriological examination of the gums showed isolated colonies of staphylococci. Examination of the stain films showed little change in the red cells; no poikilocytosis; nucleated cells not found. The small lymphocytes are present in great disproportion. The autopsy showed comparatively little enlargement of any lymphatic glands; the spleen not enlarged; interstitial nephritis, with fatty degeneration of the heart and lobar pneumonia. The examination of the bone-marrow showed the presence of large numbers of lymphocytes, with diminution in the number of polynuclear cells.

This case shows symptoms divergent from the chronic lymphatic leukæmias, and resembles rather an acute infection in its onset. The duration of this man's illness was about eleven days. From the symptoms in recent cases one is struck with the constancy of the presence of an ulcerative process in the gums and dry mouth (xerostoma) in most of the cases; in others, hemorrhges or conditions akin to those seen in scurvy. The most of the cases recently reported have been studied abroad, and perhaps the majority of them were in infants and children.

In the acute cases the differential blood examination is apt to show more large mononuclear leucocytes than were present in this case. His other symptoms, however, are I think typical.

A CASE OF BANTI'S DISEASE, WITH DIFFUSE PRODUCTIVE NEPHRITIS.

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of new york.

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It is the purpose of this paper to discuss a peculiar and interesting pathological condition, exemplified in a case of advanced productive inflammation of the liver, spleen, and kidneys.

At the outset we are confronted by the difficulty of assigning it to its proper position with complete certainty. There are four pathological conditions closely resembling each other, to three of which this case presents considerable similarity.

1. The condition which is known to the Italian authors as "Banti's cirrhosis" or "Banti's disease."

2. Cirrhosis of the liver, with secondary enlargement of the spleen. In a number of such cases there is also an anæmia of a secondary character.

3. Splenic anæmia, in which we have a marked enlargement of the spleen and a pronounced secondary anæmia.

4. Primary splenomegaly of Bovaird (*epitheliome primitive*, Gaucher).

These conditions will be described with more detail in another portion of this paper.

L. M., housewife, aged thirty-two years.

Family History. Negative. *Personal History.* Measles and scarlet fever when a child. She has had one child, who died at the age of twelve months. No miscarriages. Three years ago she had gastro-intestinal disturbances, and was told that she had a gastric ulcer. She remained in bed at that time for eight months, and was given morphine to dull the pain. She has continued to take the morphine since that time. One year ago œdema of the lower limbs developed, and has persisted. She has used alcohol, but at meals only. No history or signs of syphilis.

Physical Examination. Her general condition is poor. There is marked pallor of the skin and puffiness under the eyes. The mucous membranes are red, and the tongue is large, moist, and clean. There is marked pulsation of the vessels of the neck. There is slight enlargement of the supraclavicular nodes, but no enlargement of any other nodes.

Heart. The apex beat is felt in the fourth interspace, three and one-half inches from the median line, the heart being displaced upward. There is a systolic murmur heard at the apex and transmitted upward; a systolic murmur heard at the second left interspace and transmitted up to the clavicle; also a systolic murmur heard over the vessels of the neck, of a different character from the above two.

Lungs. At the base of both lungs there is flatness and absence of vocal fremitus. The liver percusses one inch below the free border of the ribs.

Spleen. Nearly filling the left half of the abdomen there is a mass with a smooth surface, which is tender to palpation. The anterior edge of this mass can be traced from a point two and one-half inches from the median line at the costal margin, downward, passing three-quarters of an inch to the left of the umbilicus, reaching the median line at the level of interspinous line of the ilia, and extending two and one-half inches below this line. There is a notch in this mass at a point two inches above and to the left of the umbilicus. The abdomen is distended with fluid. There is marked œdema of the abdominal walls, especially on the left side and of the extremities.

Blood Examination, by Dr. J. W. Coe. Red blood corpuscles, 2,908,000; hæmoglobin, 45 per cent.; leucocytes, 3300. Stained specimens show nothing abnormal.

The urine is yellow, turbid, of specific gravity 1015, and acid reaction. There is a trace of albumin, but no glucose or bile pigment. The sediment is composed of sodium urates and red blood cells.

The temperature ranged between 99° and 100° F., rising just before death to 105° F.

Autopsy, by Dr. A. E. Thayer. There is no rigor. The diaphragm on the right side is at the level of the fourth rib; on the left side, at the fourth space. Pleuræ, old adhesions at both apices. In each pleural cavity there are about 150 c.c. of clear serum. The bronchi contain much pus.

Pericardium. Contains about 100 c.c. of clear serum. The mitral valve is thickened, opaque, and slightly retracted. The chordæ tendinæ are thickened and short. The left auricle is dilated and hypertrophied. The large veins of the thorax are much dilated, and all the blood is fluid.

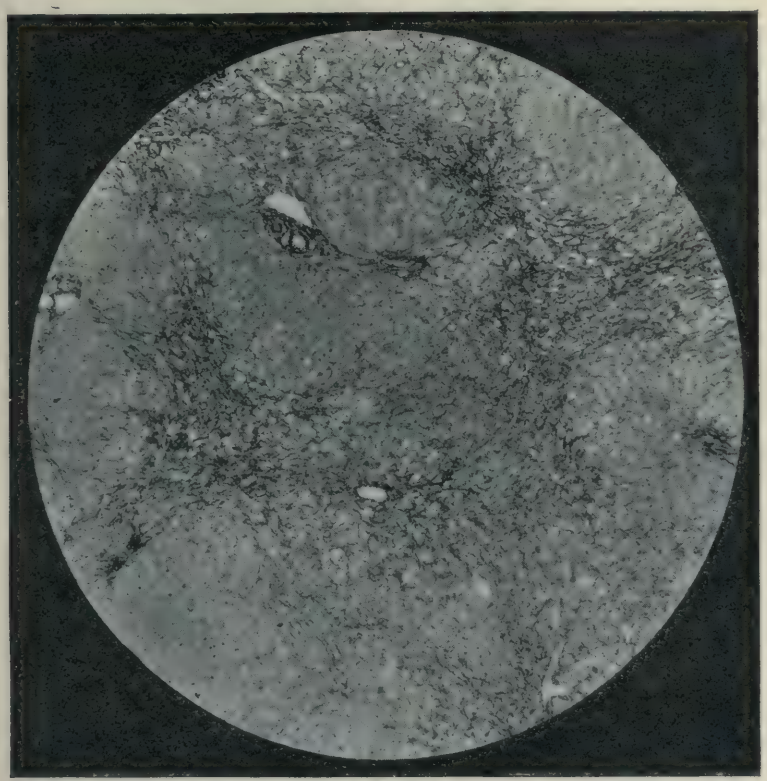
Peritoneum. There are firm adhesions between the omentum and the pelvic contents on the right side.

Spleen. Weighs 1470 grammes; is firm and dark. On section, shows a marked increase of connective tissue throughout the whole organ. The capsule is thickened, the splenic vein is much dilated. Firm adhesions prevent any movement of the organ.

Pancreas. Appears normal.

Liver. Weighs 3288 grammes; is firm and pale. The capsule is thickened and smooth. On section, this organ shows a great increase of diffuse connective tissue.

FIG. 1.



Liver showing diffuse growth of new connective tissue.

Kidneys. The combined weight is 622 grammes. They are large, firm, and pale. The cortex is swollen and anæmic, the markings irregular. The pyramids are congested; there are many punctate hemorrhages on the surface. The ureters and adrenals are normal.

Stomach. Appears to be normal. There are no scars to be found. The common bile-duct is pervious.

Intestines. Peyer's patches are swollen and congested, otherwise normal. The lymph nodes of the mesentery are swollen.

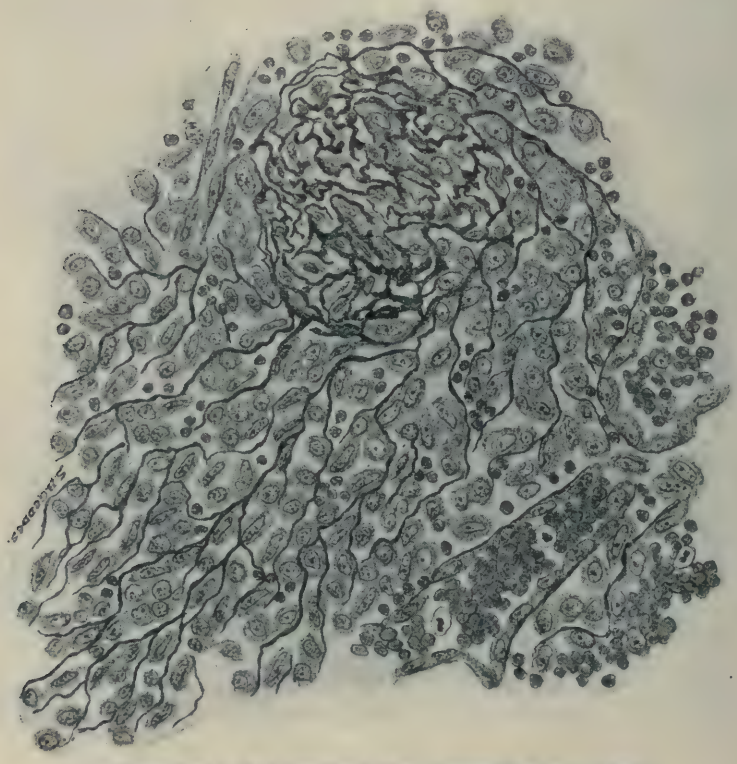
Gross Anatomical Diagnosis. Purulent bronchitis; splenic enlargement; cirrhosis of the liver; nephritis.

Microscopic Examination. Kidneys. Both kidneys show the lesions of chronic interstitial nephritis. The glomeruli appear to be normal in all respects. In some places the tubules are compressed by a diffuse

growth of new connective tissue, and in these portions the lining epithelium is degenerated. In the lower portions of the tubules their lumina are seen to be filled with a granular deposit. The bloodvessels in this organ show only slight changes. On staining sections with Weigert's elastic tissue stain it is found that a large proportion of the new connective tissue is composed of elastic fibres.

Sections from different parts of the *liver* show a pretty evenly distributed growth of new connective tissue throughout the organ, not only in the interlobular spaces, but also penetrating the lobules and even separating the individual liver cells. There is no proliferation or new formation of bile ducts, such as is commonly seen in cirrhosis, but the new connective tissue is abundantly infiltrated with small

FIG. 2.



Sclerosis of a Malpighian body. Stained same as liver.

round cells, and in places shows a slight deposit of brownish pigment. Sections stained by Weigert's method show that elastic tissue fibres are present only in their normal situations and in normal amount. The liver cells are in an advanced stage of fatty degeneration. Their nuclei stain faintly, and their protoplasm has an increased affinity for eosin.

Sections of the *spleen* show the same changes throughout the organ. There is a very great increase of the connective tissue, and in a number of sections it is seen that this increase is due to a proliferation of the normal reticulum of the splenic pulp. By the use of Weigert's elastic tissue stain it is found that a great proportion of the connective tissue is made up of elastic fibres. The Malpighian bodies for the most part show a very advanced sclerosis. In fact, some of them are represented

by nothing but a mass of connective tissue. Here and there throughout the new connective tissue there is an infiltration with small round cells. In some of the pulp spaces the lining cells seem to have undergone a slight proliferation, some of them lying free in the pulp spaces.

We sum up the pathological findings in this case as follows: 1. A marked secondary anæmia. 2. An enlarged spleen, weighing 1470 grammes, its microscopic examination revealing a very marked general hyperplastic interstitial splenitis. 3. A diffuse hypertrophic cirrhosis of the liver of comparatively recent origin. 4. A general productive interstitial nephritis.

1. Of the four conditions to which the present case bears similarity the most noteworthy is Banti's cirrhosis. Banti's disease is characterized by changes in three organs: (1) A gradual enlargement of the spleen; (2) an anæmia of the secondary type, which becomes progressively worse; (3) the later development of a cirrhotic process in the liver. The description which follows is based on Banti's three papers.

The Clinical Picture. Banti divides the course of the disease into three stages. The first he terms the pre-ascitic stage, which dates from the discovery of the first signs of enlargement of the spleen. This enlargement of the spleen may be the only abnormality present for a long time, but sooner or later the blood begins to be affected, and anæmia develops. The red blood cells are seldom under 3,000,000. The hæmoglobin index is slightly below normal. There are no changes in the leucocytes. No nucleated red blood cells are ever found. This stage may last for years, the gravity of the anæmia and the general condition of the patient varying.

The second or intermediate stage is marked by the appearance of gastro-intestinal disturbances. The anæmia becomes more severe, and the quantity of the urine, which until now has been normal, diminishes, and the excretion of urates is increased. This stage may last from a few months to a year.

The commencement of the terminal or "ascitic stage" is marked by the appearance of ascites. The fluid when removed and examined is found to be a transudate. After tapping it reaccumulates very rapidly. The excretion of the urine is markedly lessened. Its specific gravity rises to 1030 to 1040, and it is very rich in urates, and in some cases bile pigment may be present. The patient dies in the course of a few months of general exhaustion, unless of an intercurrent disease.

The Pathological Changes. The Spleen. This organ is found uniformly enlarged. The average weight in ten cases was found to be 1563 grammes, though the range in these ten cases was very wide, as is seen by the following table:

In two cases the spleen weighed	3000 gms.
In two cases the spleen weighed	1500–2000 gms.
In three cases the spleen weighed	1000–1500 gms.
In three cases the spleen weighed	623–1000 gms.

Six hundred and twenty-three grammes was the lowest recorded weight.

The picture under the microscope is the same as that observed in the present case, except in two of Banti's cases, in which we find, besides a great increase in the connective tissue of the organ, a very marked proliferation of the endothelial cells lining the pulp spaces, and the published drawings seem to be like those recently published by Bovaird in his paper entitled "Primary Splenomegaly."

The increase in the connective tissue throughout the whole organ was the only pathological change noted in the other cases. The Malpighian bodies were involved in this sclerotic process to a very great extent.

In some cases they were very markedly atrophied, and no other cellular elements were present except the connective tissue.

The Liver. The lesion in the liver was, in the majority of the cases, an atrophic cirrhosis, though in a number it was of hypertrophic type. In most of the cases the connective tissue was infiltrated with small round cells.

The Kidneys. In only two cases was the condition of the kidneys mentioned, except in a most superficial way. In the two cases in which a definite statement was made it was only said that a nephritis was present, and so I am unable to state the exact type of nephritis that occurred in these two cases. Judging from the clinical histories of the other cases it would seem that there must have been a nephritis present in a number of them.

The bone-marrow was normal in all except three cases, and in these it was stated that it had reverted to the fœtal type.

To sum up the pathological conditions present in this so-called "Banti's cirrhosis," we have: 1. An anæmia of a secondary type. 2. A very great enlargement of the spleen, due to a hypertrophy of all the cellular elements, but more especially of the connective tissue. 3. A cirrhosis of the liver, but not of a constant type. 4. An inflammation of the kidneys in a number of the reported cases.

2. *Cirrhosis of the Liver, with Secondary Enlargement of the Spleen.* The second group of cases comes under this head. We often see, in long-standing cases of cirrhosis of the liver, a more or less enlarged spleen and also very often a marked secondary anæmia. Now, in regard to the enlargement of the spleen secondary to cirrhosis of the liver I have searched the literature to find some definite figures as to the size it may reach, but have been unable to find any. It would seem, though, from the autopsy records to which I have had access, and from statements of experienced pathologists, that the spleen in this condition never reaches the size and weight of that organ as found in "Banti's disease," splenic anæmia, or primary splenomegaly.

3. *Splenic Anæmia.* The only point of dissimilarity between this condition and "Banti's disease" is that in the former the liver is normal, while in the latter that organ is found to be cirrhotic.

4. *Primary Splenomegaly.* This term should be reserved for those cases which present a splenic lesion similar to that described by Bovaird.[18] In his case the splenic enlargement was due to a very great proliferation of the endothelial cells lining the pulp spaces, and the increase in the connective tissue elements was but nominal. The clinical picture as appearing in his description is very like that of the other conditions.

Differential Diagnosis. We may differentiate between cirrhosis of the liver with secondary enlargement of the spleen and the three other conditions—namely, "Banti's disease," splenic anæmia, and primary splenomegaly—by the following facts: 1. The spleen in cirrhosis of the liver never attains the size that it does in the three other conditions. 2. The anæmia in cirrhosis is apt to be less severe than in the other conditions. 3. In cirrhosis the splenic enlargement is secondary, while in the other conditions it is the primary lesion.

This last point is of very slight diagnostic value, as the vast majority of the cases is not seen until too late a stage of the disease, and, as Osler[16] has pointed out, we cannot be sure of the presence or absence during life of a cirrhotic process in the liver.

The diagnosis between splenic anæmia and primary splenomegaly can only be made by microscopic examination of the spleen, as there is no difference in the conditions except that in splenic anæmia the increase in size of the organ is due to a general hyperplasia of all the cellular elements, but more especially of the connective tissue; whereas in primary splenomegaly the increase is due to a very great proliferation of the endothelial cells lining the pulp spaces, with only a moderate increase in the connective tissue.

The only point of difference between "Banti's disease" and splenic anæmia is that in the latter there is no cirrhosis of the liver; therefore we may say that "Banti's disease" is splenic anæmia plus a cirrhosis of the liver.

Conclusions. 1. There are four conditions, more or less closely related, which may be distinguished as follows: Enlargement of the spleen with anæmia and the later development of a cirrhotic process in the liver may be separated from cirrhosis of the liver, with secondary enlargement of the spleen, by the fact that in the latter condition the spleen never attains the size that it does in the former. Both these conditions may be separated from splenic anæmia and primary splenomegaly by the presence of the cirrhosis of the liver, while these two latter conditions may only be differentiated from one another after a microscopic examination of the spleen.

2. The case here reported should be placed among those cases termed "Banti's disease" for three reasons: (*a*) The very great enlargement of the spleen; (*b*) the presence of a cirrhotic process in the liver; (*c*) the fact that the enlargement of the spleen was due to a general hyperplasia, but more especially of the connective tissue.

3. The present case, exhibiting an advanced chronic productive nephritis, somewhat extends the scope of the pathological anatomy of Banti's disease.

Speculation as to the etiology of the disease seems at present premature, but the increasing recognition of the occurrence of transitional cases connecting together Banti's disease, splenic anæmia, and diffuse cirrhosis of the liver suggests an origin from a common cause emanating from the gastro-intestinal tract.

Finally, I would thank Prof. James Ewing for placing this case at my disposal, and for many kind suggestions during the preparation of this paper. For the photomicrographs I am indebted to Dr. B. H. Buxton.

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ARTICULAR RHEUMATISM AND SOME ALLIED CONDITIONS.[1]

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GENTLEMEN: I shall bring before you a number of cases illustrating various types of joint disease having a more or less superficial resemblance and requiring careful study to determine the pathology and diagnosis. First I wish to present two cases of acute articular rheumatism.

[1] Clinical Lecture delivered at the Pennsylvania Hospital.

Case I.—Charles F., a negro, aged thirty-five years, a cook, was admitted to the hospital on October 8th, giving us the following history. His parents died of old age; he has had ten brothers and sisters, all of whom are living and in good health.

He himself had measles in childhood, and somewhat later malaria. Several years ago he was injured, as a result of which his left elbow has remained enlarged and stiff.

His present illness began four days before admission, when he was taken with a sudden chill. This occurred in the night, while he was at his work; the next morning his ankles, knees, wrists, and elbows were painful and somewhat swollen. The subsequent day the right side of his face became swollen and painful. He has not suffered with extreme pain.

On admission to the hospital we found some swelling of the joints mentioned, but particularly of the left wrist and elbow and of the right side of the face. His temperature was 100.3° F., and he complained of rather severe pain in the affected parts.

On examination the swelling of the right side of the face was found to centre about the temporomaxillary joint, the slightest movement of which caused extreme pain. Surrounding this as a centre there was a rather tense infiltration of the soft tissues, with sufficient heat to indicate an inflammatory process. The left elbow and wrist were swollen, as well as painful and hot, but there was no fluctuation. The left knee was painful, but little if at all swollen. The other joints first mentioned were a little tender on movement, but otherwise unaffected.

Physical examination of the chest showed normal conditions, excepting that the heart was slightly enlarged to the right and to the left. No distinct murmur was heard. The pulse was of good volume and regular. His urine was dark, amber-colored, acid, specific gravity 1020; it contained no albumin or sugar. On microscopic examination amorphous urates and leucocytes were found.

His condition to-day, as you will see, is little changed, although the joints have improved since his admission. The side of the face is still sufficiently swollen to be visible at a distance, and as I examine the parts carefully I detect the centre of the swelling to be in the temporomaxillary joint, and he complains of pain on any movement of the jaw. The soft tissues around the joint are swollen as far forward as the angle of the mouth and downward to the ramus of the jaw. The parotid gland does not appear to be specially enlarged. The infiltration, therefore, seems to be superficial. The knees and ankles are scarcely if at all enlarged or tender, and there remains only a rather considerable degree of pain and swelling of the left elbow. The enlargement of this joint is evidently not acute, as the joint is partially ankylosed, doubtless as a result of the injury sustained many years ago. The tenderness, however, is greater than an old joint trouble of this sort would occasion without the intervention of an acute disease.

I wish to direct your attention to one of the more interesting points in this case before presenting another case and taking up the discussion of the disease in general. I wish you to note that the onset of the illness in this man was marked by a sudden chill, without any premonitory

symptoms, and the affection of the joints was sudden. The large joints alone were involved—ankles, knees, wrists, elbows, temporomaxillary joint; the small joints — metatarsal, metacarpal, phalangeal — all remained free.

Case II.—G. F., aged twenty-five years, a native of Italy, and a laborer, was admitted to the hospital October 12, 1901. We could obtain little history from him.

Three days before admission his joints became painful, the knees and ankles first being affected, and later the right elbow and the wrist. He also complained of stiffness in the neck, locating the trouble as nearly as we could determine in the muscles at the back of the neck rather than in the vertebral joints.

His condition now is practically the same as on admission. You see he is a well-nourished man. The tongue is a little coated; his temperature has been normal from the day of his admission. There is considerable swelling of his right wrist, and despite the dark color of his skin the redness of the surface is quite apparent. No distinct fluctuation, but a boggy resistance is offered to the palpating finger. The joint is evidently very tender, as the slightest movement causes pain.

On examining his heart I find the right border beneath the right border of the sternum. The apex extends as far to the left as the midclavicular line. The upper border is beneath the third rib, and the lower border under the sixth rib. The apex impulse is strong and regular. On auscultation I discover a peculiar alteration of the first heart sound, which may be described as prolonged, vibrating, or murmurish; indeed, at times there seems to be a distinct murmur separate from the heart sound. These characters are noted at the apex, but not at a great distance from it, either toward the axilla or toward the base of the heart. At the pulmonary area the second sound is a little accented; otherwise, the auscultatory phenomena are normal.

Further physical examination is negative. The urine is amber-colored, acid, specific gravity, 1022; it contains neither albumin nor sugar. On microscopic examination some epithelial cells were discovered.

A matter of special interest in this case is found in the auscultatory phenomena relating to the heart. The peculiar alteration in the first heart sound is one which is always highly suggestive when occurring in rheumatism and one which requires most earnest consideration. I shall refer to this later.

Case III.—The woman whom I now show you presents the conditions of the joints found in articular rheumatism in a rather more acute stage than was seen in the two other cases. Her present attack began a week ago with fever and painful swelling of the knees and ankles, as well as of some of the joints of the hands. As you see, the right ankle, and to a less extent the left, is swollen and red. There has been much more redness, which has given place to pigmented spots and diffuse pigmentation of the skin. On pressure the tissues pit slightly and have an elastic, infiltrated feeling. The skin is stretched, and therefore smooth. Similar conditions are visible and palpable in

the right knee. The contrast with the left knee is quite striking. The history and other physical conditions of this patient need not detain us longer.

I show these cases as instances of typical mild, acute, articular rheumatism. They do not present all of the characteristic or cardinal symptoms, but sufficient for the purpose of diagnosis, and serve very well to introduce the subject of this disease for our consideration.

What is acute articular rheumatism? In the light of our present knowledge we may define it as an acute infectious disease of sudden onset characterized by enlargement, pain, and redness of several of the

FIG. 1.



CASE I.—Acute articular rheumatism, showing redness, swelling, and infiltration of the joint.

larger joints and sometimes of the smaller joints, attended with mild or severe irregular fever, fluctuating more or less with exacerbations in the articular manifestations and accompanied by a tendency to acid sweats and highly acid urine. The joint affection is characteristically polyarticular, usually begins in the large joints of the lower extremity, subsequently involving the upper extremities and often the small as well as the large joints, and commonly exhibiting a tendency to rapid subsidence in one joint, with equally sudden appearance in another. The specific cause of rheumatism, if there be a single specific cause, is unknown, and there is nothing peculiar in the pathology of the joint affection or of the complications by which rheumatism can be

absolutely distinguished. The disease must be recognized by the clinical syndrome; it is a "symptom complex" rather than a definite disease, as far as we are now able to define it.

Theories regarding acute articular rheumatism have been numerous, and the history of the affection is as old as the history of medicine. I shall not now delay to discuss the older chemical theories which have practically disappeared, excepting in the still somewhat prevalent views regarding matters of treatment; and I shall reserve for a later part of these lectures a consideration of the rôle of the nervous system in rheumatism and rheumatoid diseases.

The most advanced authorities in all parts of the world concede that the disease is an infection. This is manifest in the similarity of its onset to that of the infectious diseases, as shown by the first case I have exhibited. It is further evidenced by the peculiar character of the joint affection and particularly by the complications, notably endocarditis. Bacteriologists have occupied themselves with the investigation of the blood, tissues, and excretions of rheumatic patients and a variety of organisms have been discovered. The majority of those who have investigated this side of the question have found some form of micrococci, either staphylococci, streptococci or diplococci; but various bacilli, aërobic and anaërobic, have been discovered in certain cases. Widely varying results have attended examinations of the synovial fluid, of the excretions, and even of the tissues of the joints.

Of particular interest are the cases in which the same micro-organism has been discovered in the joints and in the endocardial vegetations that are recognized as secondary to the joint disease. Great interest also attaches to the joint lesions and endopericardial lesions produced in animals by injection of pure cultures of micrococci or bacilli isolated from cases of rheumatism. The importance of these observations has, however, in my estimation been exaggerated. Clinicians and pathologists regard staphylococci, streptococci, and other micro-organisms as among the bacterial causes of pleurisy, but no one would expect to prove this relationship by producing pleurisy in animals by intravenous injections of cultures of these germs from cases of pleurisy. It will be admitted upon grounds of analogy and general pathological knowledge that joint lesions would be likely to follow sepsis produced by injection of streptococci of whatever source; the occurrence, therefore, of such lesions does not establish for any particular culture of streptococci or diplococci a specific relation to rheumatism. It is idle to say the joint lesions resemble those of rheumatism. Acute inflammations of all kinds have so much resemblance in the joints that this argument is of little weight.

It is very clear that no organism thus far discovered can be looked

upon as in any sense the specific cause of this disease. It is not impossible that, like pneumonia and other infections, a variety of organisms may occasion pathological and clinical manifestations sufficiently similar to be grouped under the same heading or name. The problem of determining from the point of view of etiology the nature of articular rheumatism and its right to the station of an independent affection becomes much more complicated when we recall the number of diseases with which arthritis of a closely allied type associates itself. The articular manifestations resulting from or attending gonorrhœa are best known and are most often referred to in this connection, so much so that the term "rheumatism" is often applied without much reservation. Very similar involvements of the joints may occur in connection with scarlatina, typhoid fever, dysentery, smallpox, pneumonia, and septicopyæmia. In all of these there is a greater tendency to a limitation of the disease to one or a few joints, and generally there is a greater permanency of location during the continuance of the malady. Further, these joint affections are more prone to terminate in suppuration and extensive destruction of the joint, and the other clinical features, mild remittent fever and acid sweats, are for the most part absent. A typical instance of gonorrhœal arthritis or pyæmic arthritis would not readily be mistaken for a case of acute articular rheumatism, but there are many instances of milder arthritides in association with this or other infections in which the clinical characters could not be relied upon to distinguish the affection from rheumatism. It is these considerations which have led some of the more radical and advanced internalists to discard the distinction between acute articular rheumatism and the joint diseases attending other infections, and some have proposed to call such cases pseudorheumatism or rheumatoid diseases. According to these authorities all acute infectious joint diseases should be considered together as one group of "infectious arthritis," whether for the sake of convenience of clinical study and discussion, a distinction between polyarticular arthritis (common rheumatism) and a monarticular or pyæmic arthritis be made or not. Other authorities, like Chvostek, following the same line of reasoning, insist that acute articular rheumatism is not a disease sui generis, but merely a symptom complex which may have a variety of causes. Many others who would not go to the length of discarding acute rheumatism as an independent disease admit the close relationship of rheumatism to the arthritides of definite infectious diseases and maintain a position of hopefulness of the discovery of a specific microbe which shall relieve the situation of all further embarrassment. In the meantime, however, a careful review of existing knowledge must convince us that at the present day no sharp line can be drawn either clinically or pathologically between the joint diseases attending definite infections and that form of joint disease

which usually presents rather distinctive clinical characters and usually arises without a distinct pre-existing infection, and which we know as acute articular rheumatism. We must still further admit that while it is not as a rule the sequel of any infection but is a cryptogenic infection, there are certain cases in which a pre-existing infectious tonsillitis or other infectious process immediately precedes the rheumatic fever.

I recall as I speak an interesting case under my care at the Philadelphia Hospital some years since, that of a young man who was admitted to the hospital with typical acute articular rheumatism affecting the right wrist, the left elbow and wrist, and knees. The process had begun in the right wrist, and this joint was considerably more swollen and painful than any of the other joints. The onset of the trouble was sudden, and was apparently the direct result of an infected wound of the dorsum of the right hand. The patient had suffered a lacerated wound of his hand a week or ten days before the onset of the rheumatism and several stitches were introduced, but the after-treatment was neglected and at the time of his admission to the hospital a crust had formed over the wound, and beneath this was found a drachm or more of pus. The rheumatism rapidly subsided after relief of the original focus of infection.

Another case in my experience was that of a nurse at the Howard Hospital who was under my care for acute follicular tonsillitis. The crypts of the tonsils were distended with yellowish-white, creamy material, and there was an extensive associated pharyngitis. In the midst of the attack of tonsillitis she developed acute articular rheumatism which ran through a typical course.

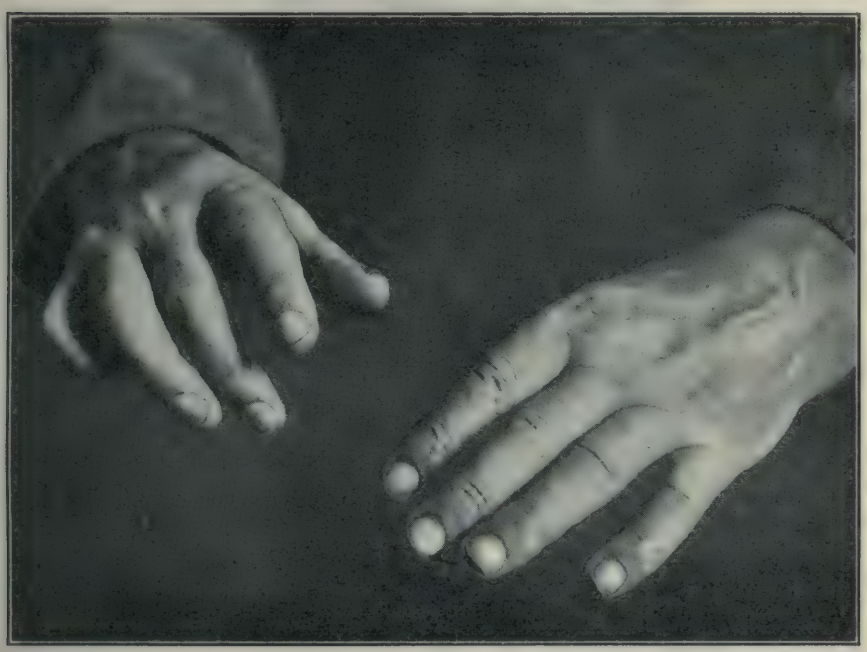
Instances like these show that while, as a rule, rheumatism is cryptogenic it is not always so. This fact is based not upon isolated cases such as those I have quoted, but upon the experience of many others who have observed the connection particularly between rheumatism and a preceding tonsillitis. It must, of course, be admitted that in the absence of a known specific cause by which the joint affection and the pre-existing infection can be identified as part of the same process, those who maintain that the primary disease merely predisposes to the incidence of rheumatism are entitled to their view if they can show that such disease is in any way of importance as a predisposition.

I shall not dwell longer upon this important question of the nature and etiology of rheumatism, but I could not dismiss the subject with fewer words because I wished to impress upon you the importance of forming clear ideas as to the limitations of our knowledge regarding this group of affections. As I go further in the exhibition of cases, and show you instances of joint disease of other sorts, more or less related to rheumatism, you will appreciate how difficult the subject is and how incomplete as yet is our knowledge.

Case IV.—The next case which I shall show you is one whose history is somewhat indefinite so far as the exact symptoms of onset and the evolution of the disease are concerned, but which we at least know is of chronic character. The patient tells us that he has been suffering with progressive involvement of the joints running back to a period two years ago.

As you see, certain of the joints of his right hand are greatly enlarged and present a more or less globular or rounded appearance (Fig. 2), and the term globular rheumatism might be applied to this condition if the same name had not been used in connection with another form of rheumatoid disease which I shall have occasion to refer to later. This form of chronic rheumatism, which is quite well illustrated by this case, is in my experience rather more common in children than in adults, but it does occur, as a matter of fact, at any age. The photo-

Fig. 2.



Subacute or chronic articular rheumatism.

graph (Fig. 3) which I am passing around is one taken from a case under my care at the Children's Hospital.

Any of the joints may be involved, but the more characteristic lesions are those affecting the smaller joints of the hands and feet. The interphalangeal joints and the metacarpophalangeal joints become more or less uniformly enlarged and greatly indurated and stiffened. You see this condition in the patient before you. On palpation of these joints I find that there is no bogginess, no evidence of effusion such as is common in acute rheumatism; there is no redness, and the patient complains of comparatively little pain. In addition I find on attempting to flex and extend these joints that the process has gone on to almost complete ankylosis. A little movement, however, is preserved, and on exercising this I find no grating or friction of any sort; simply the resistance

offered by a joint stiffened with fibrous adhesions. This constitutes the essential morbid anatomy of the condition before us.

As you see, the affection of the joints in this man is not symmetrical; the right hand is much more involved than the left, but the knees and the ankles of the two sides are almost equally and quite similarly affected. The skin of the hands, feet, and legs over the affected parts presents no abnormalities; it does not show the trophic changes so common in the form of joint disease which I shall presently discuss with you.

FIG. 3.



Chronic articular rheumatism, with nodular enlargement of interphalangeal joints.

Chronic rheumatism of this type is essentially the sequel of acute articular rheumatism. It is more frequent in those who have suffered repeated attacks than as a consequence of a single attack, however severe. We are, therefore, likely to find this form of chronic joint affection associated with chronic cardiac disease, for you will find endocarditis or endopericarditis and recurring rheumatism is a not infrequent association. Whether in these instances the endocardium continues to be affected by a subchronic form of inflammation or whether there are recrudescences of acute endocarditis from which infective material is thrown into the circulation, with consequent recurring disease of the joints, cannot be asserted. The clinical association, however, is well recognized, and it is in the cases in which this association occurs that diffuse or polyarticular chronic rheumatism of the type here presented most frequently presents itself.

Chronic rheumatism of a monarticular kind is, as you are probably aware from your personal experience, a not infrequent condition in aged people. In these cases some one joint, as the hip, elbow, or shoulder, may be stiff and more or less painful, becoming especially so in the colder and more changeable seasons of the year. Going back to the onset of the trouble we very often find in these instances a history of acute rheumatism involving a number of joints with persistence of the trouble in one joint which has become permanently affected and perhaps slightly ankylosed. These cases are of less interest in connection with the disease which I shall show you presently, that is, rheumatoid arthritis, than are the cases of polyarticular rheumatism. An exception might perhaps be made in the case of a form of chronic rheumatism affecting the hip-joint, as there is a variety of rheumatoid arthritis confined to the hip-joint that has a puzzling resemblance to simple chronic rheumatism.

I stated in the beginning that the history of onset in the case before us is somewhat uncertain. Most of these cases begin with acute symptoms, and after pursuing a clinical course not dissimilar to that of other cases of acute rheumatism, they terminate in a gradual chronic change or in a succession of relapsing attacks of milder character until the chronic changes in the joint are effected. There are cases, however, in which the history of onset is that of a chronic process from the start, and to this group we must assign the case before you if the history the man gives us is reliable, and there is no special reason to doubt his statements.

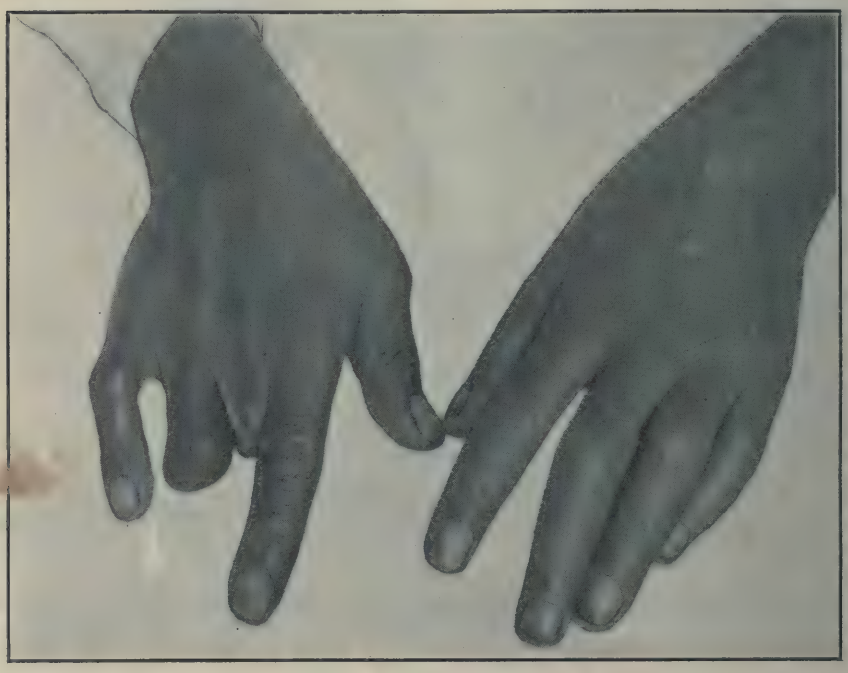
Certain varieties of nervous diseases are of interest in the present connection because of the association of diseased joints. You are familiar with the arthropathies that have been collectively described under the name of the "Charcot joint." In this condition a single large joint is usually involved and the association with a chronic spinal disease is direct and usually clearly recognized. This, however, is not the kind of joint disease that I have specially in mind at this moment. There are other and less distinctive affections of the joints in connection with various nervous diseases, causing loss of power and consequent lack of use of the joints. Perhaps the affection of the nerves and of the central nervous system plays a direct part in the changes in the joints. Of this we cannot always be certain. Such joint conditions occur in various cerebral and spinal diseases, and also in neuritis. The joints of the affected parts enlarge and become ankylosed to a greater or less degree. In part the enlargement of the joints may be only apparent and due to atrophy of the surrounding soft parts; in the later stages, however, there is definite enlargement and disease of the joints. Among the nervous diseases in which this sort of joint disease occurs are cere-

bral palsies with late rigidity, poliomyelitis, spastic palsies of various sorts, and, as I have said before, neuritis.

Case V.—I shall now present a case presenting this condition (Fig. 4). The appearance of the affected hand may be compared with the same hand in a case of acute articular rheumatism (Fig. 5) to show the marked resemblance.

The patient, a negro woman, fifty years of age, has been in the hospital for several months. Her illness began rather suddenly, with pain in the left arm and tenderness along the nerve trunks. It was soon recognized that she was suffering with neuritis; but early in the case the wrist-joint became enlarged and tender, and simulated in its appearances the conditions seen in acute rheumatism. The disease, however, has been afebrile, limited to the left wrist and hand, and associated with

Fig. 4.

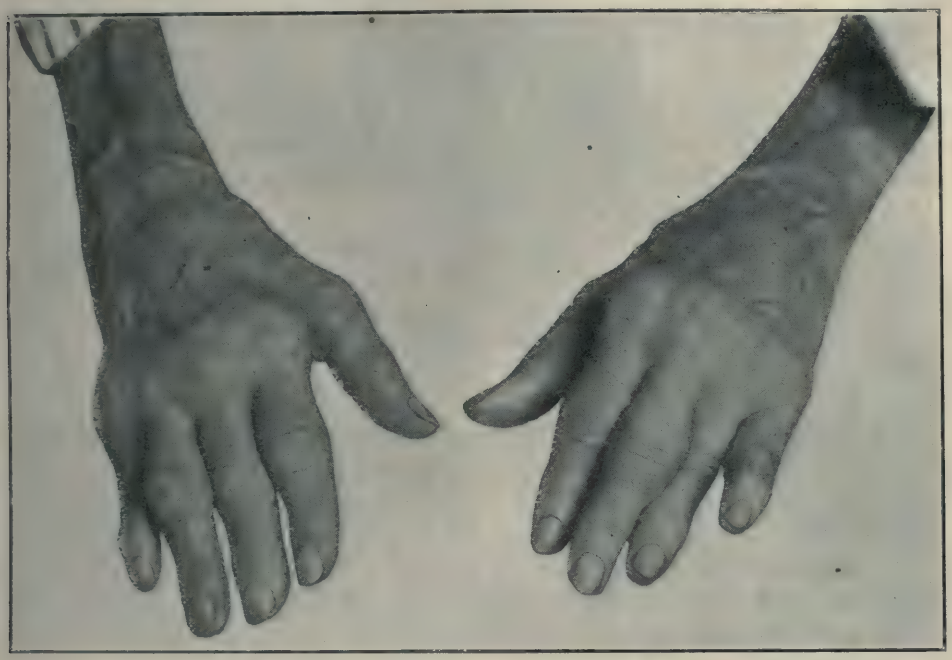


Joint lesions in left hand resulting from neuritis.

general œdematous swelling of the forearm and hand, and with continued evidences of neuritis. There could be little doubt, therefore, that this case was not in any sense rheumatic. As you see her hands to-day, there is a marked contrast between the left and the right hand, which has been mutilated by an accident. The back of the hand and arm are less swollen than they have been, but the fingers and the phalangeal joints are still considerably involved. A bilateral involvement of this sort, or, still more, one affecting the legs and feet, as well as the upper extremities, would easily confuse diagnosis by simulating rheumatoid arthritis or chronic rheumatism of the type I have described in connection with the last case. A case of this sort recently under my observation had been treated as one of rheumatoid arthritis. The disease was essentially a nervous affection, a chronic poliomyelitis, and the

joint disease was secondary. I have seen the same mistake in cases of alcoholic and arsenical neuritis. Perhaps it does not make much difference in the ultimate outcome of the condition whether a proper diagnosis is made or not; but a considerable amount of salicylate of soda might be saved, and I am not sure but that frictions and manipulations would, as in the woman before you, accomplish a very satisfactory though slow result.

FIG. 5.



Acute articular rheumatism of the hands.

I have introduced these forms of nervous affection of the joints on account of their resemblance to the rheumatoid disease. They must not be regarded as in any sense rheumatic.

The next subject to be referred to, viz., rheumatoid arthritis, is probably closely allied to the nervous affections, but is not so clearly the result of definite nerve disease.

Rheumatoid arthritis, rheumatic gout, gouty rheumatism, deforming arthritis, arthritis deformans, osteo-arthritis—all these terms have been used to designate the type of disease which is illustrated by the woman whom I bring before you. This is a condition met with very commonly in hospitals where aged persons form a considerable proportion of the patients, and it is usually considered among the diseases of old age; indeed, its discussion occupies a considerable part of that most interesting clinical work by Charcot, *Clinical Lectures on the Diseases of Old Age*. Much of our knowledge of the disease has been contributed by this eminent clinician. While it is thus customary to consider it essentially a disease of old age, it is well to observe that rheumatoid arthritis not infrequently arises in persons in the second or third decade of life,

but as the affection is essentially a chronic one, many of these persons live to advanced years, and eventually may find their way into institutions for the aged.

The history of the case before us is as follows:

Case VI.—Nora C., aged forty years, had had measles, whooping-cough, and typhoid fever in childhood. There is no history of other illnesses. She was married at seventeen and had one child.

She was in good health until the early part of 1900, when she complained of slight pain in the left knee. Later the ankles and occasionally the heels were affected. She improved and then had recurrences at intervals. The hands became affected later, and deformity of the fingers did not begin until a short time before admission to the hospital. Before the onset of the rheumatic symptoms she had begun to lose flesh and had a poor appetite.

When admitted she was emaciated in appearance and old beyond her years. The skin was sallow and dry. The ankles were swollen and tender, but not red. There was no œdema of the feet or legs. Examination of the hands showed a marked ulnar deflection of the fingers on both sides, and considerable swelling and tenderness of the ends of the metacarpal bones.

Examination of the heart disclosed no symptoms or abnormal signs excepting a slight accentuation of the second aortic sound. There was a little congestion at the bases of both lungs. The urine was normal.

On re-admission to the hospital, in 1901, the hands were more distorted, and the ulnar deflection was found very marked. The interphalangeal joints were more strikingly affected. The wrists were greatly enlarged, though the motion was still fairly good. The knees had become very much enlarged, and the right was quite painful. The feet were swollen and œdematous. The ankles much enlarged. She could walk with difficulty. The urine was now found to contain a trace of albumin and a few granular casts.

Examination of the blood showed a slight anæmia. Gouty tophi were looked for, but were wanting. Subsequently there was fluctuation in the degree of pain and tenderness, as well as in the swelling about the affected joints.

In the early part of her illness she frequently had moderate fever, though never very continuously. In the later part of her illness the temperature had been normal almost continuously.

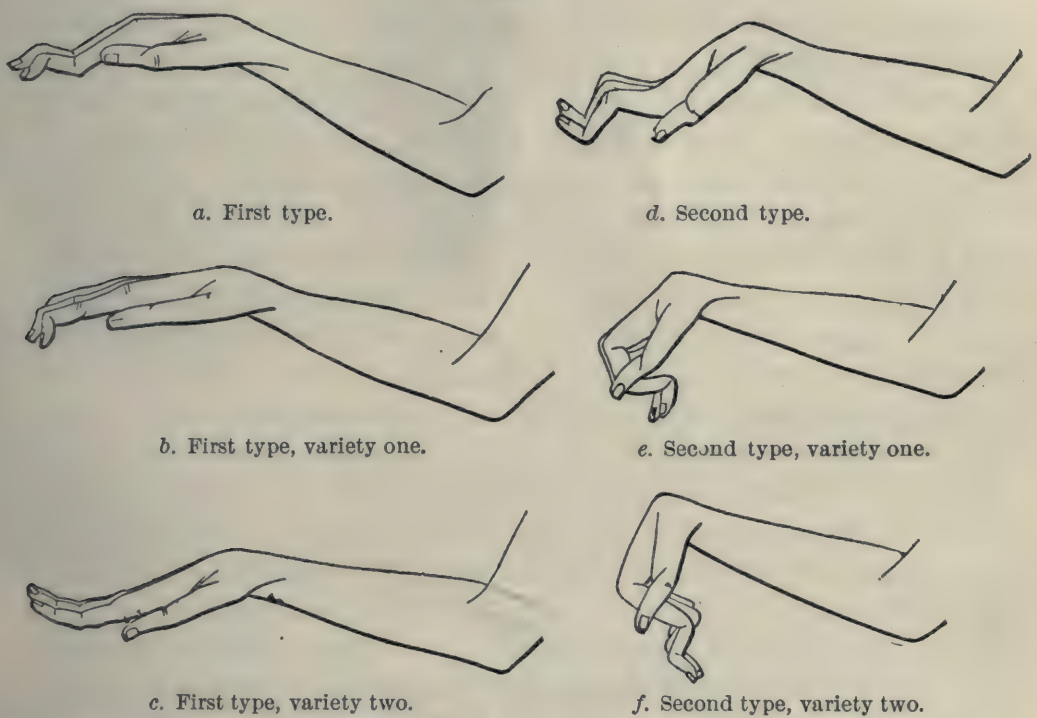
Rubbing and tonic treatment caused some improvement, so that she is now able to walk a little.

The history and the clinical features in this case are rather characteristic. The disease begins without acute manifestations, and advances in a more or less progressive manner without acute exacerbations. Occasionally, it is true, the onset may be abrupt and the course of the disease may be marked by acute attacks, each of which increases the affection of the joints. The case before us, however, is fairly typical in character; the onset was gradual, the course has been progressive, and the deformity of the joints has gradually increased.

It is characteristic of rheumatoid arthritis that the affection is more

or less symmetrical, as you see it here. This statement, however, must not be interpreted too rigidly, for you will frequently find minor variations on the two sides, but rather more frequently you will see that the same joints of the two sides are affected and that the progress is about equal. The character of the deformity of the hands was so well described by Charcot and so well pictured in his work that a copy of his illustration is not uninteresting (Fig. 6). He described two types of deformity. In the first there is flexion of the terminal phalanx on the middle phalanx, extension of the middle upon the proximal phalanx, flexion at the phalangometacarpal junction, and flexion at a less obtuse angle of the metacarpus and carpus on the

FIG. 6.



a. First type. *d*. Second type.

b. First type, variety one. *e*. Second type, variety one.

c. First type, variety two. *f*. Second type, variety two.

joints of the forearm. In a large proportion of the cases there is in addition an inclination *en masse* of all of the phalanges toward the ulnar side of the hand and a twisting in the opposite direction of the middle upon the proximal phalanges. Two sub-varieties of this type of deformity are observed. In the first the proximal and middle phalanges are in the same plane, while in the second variety the terminal phalanges are not flexed upon the middle phalanges as in the common type. The second type of deformity shows extension of the terminal phalanges upon the middle phalanges, flexion of the middle upon the proximal, and extension of the proximal upon the metacarpal heads. The flexion at the wrist-joint is more marked than in the other type. In certain cases of this type the proximal phalanges are de-

viated *en masse* toward the ulnar side of the hand. This type, like the first, has two varieties, in one of which there is flexion of all the articulations of the hand so as to make a kind of scroll, while in the second there is extension of the middle upon the proximal phalanges.

Next to the hand the condition of the foot is of greatest interest. Here we find ankylosis at the tibiotarsal junction very common. The foot may be adducted so as to rest upon the external border, or, on the other hand, may be carried outward. The great toe is usually deflected outward so as to cover the other toes.

While the small joints of the hands and feet are most frequently involved in rheumatoid arthritis, the disease sometimes implicates the larger joints by preference and frequently affects these joints after the small joints have been involved. Flexion with more or less ankylosis of the elbow, stiffening of the shoulder, flexion with ankylosis of the knee, and occasionally involvement of the hip, are observed. Of particular interest are the instances in which the joints of the spinal column become affected. This is most frequent in the cervical vertebræ, and it not uncommonly happens that the head is bent forward and so flexed upon the sternum that the chin nearly touches the chest. The movements of the head may be extremely limited and attended with crepitating or crackling sounds. Sometimes a similar involvement of the whole spinal column, together with some stiffness of the hip-joints, may occur without any involvement of other articulations.

The joint affections described, all of which were recognized by Charcot, constitute the conditions usually found in this disease, but there are cases of rheumatoid arthritis of limited extent and presenting such aberrant features that the diagnosis could not usually be made without a knowledge of the pathological conditions discovered in similar cases. Of this character is the joint affection of the aged, sometimes called *morbus coxæ sinilis*, or the hip disease of the aged. In these there may be entire freedom of other joints and a clinical history so uncertain that the relationship of the condition with ordinary rheumatoid arthritis would not be readily suspected. Pathological examinations, however, have shown that the two conditions are essentially the same.

Another affection which seems to belong in the group of rheumatoid arthritis is that which has been spoken of as Heberden's disease or Heberden's nodosities. This, as Charcot pointed out, is generally confounded with gout by physicians, and is practically always so regarded by the laity. It differs from gout in many particulars, as Heberden himself pointed out. The nodes have their seat at the articulation of the terminal phalanges and cause little deviation of the extremity of the digit to either right or left. There are two nodules on a level with the joint, and the joint itself seems but little enlarged. On examination there is usually rigidity, but no crepitation. The

advent of this condition is generally insidious, though at times there may be heat and pain and temporary swelling. It is these attacks which the patient often recalls as gouty. In Charcot's examinations at the Salpêtrière he found the changes of a dry arthritis, with a velvety change in the articular cartilages. The articular surfaces were enlarged in all directions on account of the formation of osteophytes, and the small tumors described by Heberden are nothing but small osseous tubercles occasionally found in this situation, but enlarged from apposition of new osseous layers. He could discover no trace of uratic deposit such as is characteristic of gout. The other joints presented similar changes, though less marked.

A few words with regard to the nature of this peculiar affection which has been the enigma of rheumatic diseases. Some of you may recall that a nervous theory has been held to explain the manifestations of rheumatism in most or all of its varieties. This theory was originated by Dr. John K. Mitchell, the father of Dr. S. Weir Mitchell. The cases under his observation were undoubtedly, however, in part instances of nervous disease, and especially diseases of the spinal cord, with association of those curious forms of disintegration of the joints now so well known under the name of arthropathies; in part the cases he observed were probably instances of rheumatoid arthritis. Even in ordinary articular rheumatism, however, there are conditions which at times would justify a suspicion of a nervous influence. In its later stages atrophy of the muscles surrounding the affected joint is not an infrequent symptom, and trophic alterations in the skin and even in the affected muscles may be observed. These changes in part are the result of disuse and the tension or stretching of the previous inflammation; in part, however, they are probably the result of implications of the peripheral nerve trunks—a true neuritis with its consequences. Nothing, however, in the history or course of the malady would indicate that this neural condition initiates the affection of the joints; on the contrary, all of the evidence clearly demonstrates that the involvement of the peripheral nerves is secondary to the disease of the joints and dependent wholly upon contiguity to the inflamed area. In the case of rheumatoid arthritis, however, conditions seem to be different. The history of cases of this malady shows plainly and almost in every instance the operation of influences the result of which must be a deterioration of nerve force and loss of vitality, and the clinical course of the disease is one which is entirely compatible with the theory that primary changes in the nervous system, either at the periphery or centrally, constitute the true essence of the pathology of the disease.

In a few instances neuropathologists have found slight changes in the nerve cells of the anterior horns of the gray matter of the spinal cord or elsewhere, but whether these have been cases of uncomplicated

rheumatoid arthritis or instances of disease of the nervous system complicated with rheumatoid arthritis, or whether, in the third place, the changes discovered were artefacts or accidental conditions, cannot be positively asserted. It would be unwarranted to say that changes in the central nervous system are found with regularity in this disease, but there can be little question that nervous changes of some sort are habitual, as is evidenced by the peculiar type of change in the joints themselves, which is progressive, painless, dystrophic, and by the evident trophic alterations in the skin of the affected parts. Notwithstanding these considerations, however, certain investigators, notably in England, have claimed the discovery of micro-organisms in rheumatoid arthritis. These claims, however, do not merit serious consideration.

In connection with this matter, I may, perhaps, profitably call your attention to the fact that micro-organisms of different kinds frequently gain entrance to the tissues and invade practically all parts of the body in the terminal stages of chronic diseases, so much so that a distinguished clinician has laconically stated that chronic diseases terminate by acute infection. In many instances in which the discovery of bacteria in the tissues has been reported, this terminal infection would explain the presence of the organisms rather than a specific nature of the disease under investigation.

TWO CASES OF COMPLETE BILATERAL DUPLICATION OF THE URETERS.

By A. H. Gould, M.D.,
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(From the Clinico-pathological Laboratory of the Massachusetts General Hospital.)

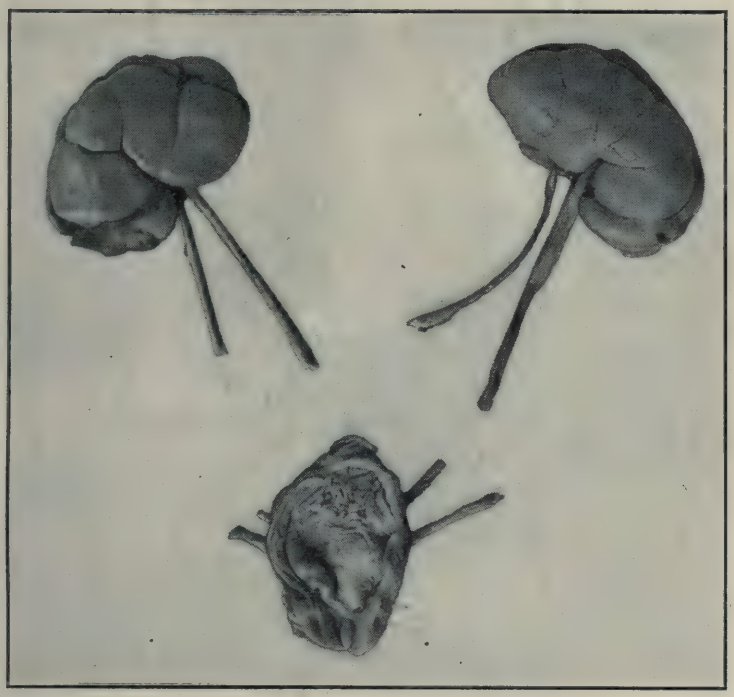
While anomalies of the ureter of one kidney are comparatively common, anomalies of the ureters of both kidneys are comparatively rare, and complete duplication of both ureters is very rare. By complete duplication is meant that both kidneys have each two ureters, and each ureter is separate throughout, having its own orifice in the bladder.

After a search through the literature only eight cases of complete bilateral duplication of the ureters were found. In collecting these cases we have excluded certain cases of bilateral duplication in which the duplication on one side was not complete, the ureters either joining together to form a single ureter, or having a common orifice in the bladder. The rarity with which the complete duplication has been reported seems to be a reason for reporting two more cases.

Case I.—A child, aged six months, dead of marasmus. Autopsy by Dr. J. H. Wright, October 9, 1899. Each kidney had two pelves and two ureters, which were separate throughout their lengths, each having its own orifice in the bladder. One ureter on each side had its orifice apparently in the normal position, while the other two ureters had their orifices nearer to the median line and nearer the prostatic urethra. One of the two pelves of each kidney was larger than the other. The kidneys proper were not remarkable.

Case II.—A woman, aged fifty years, dead of strangulated inguinal hernia. Autopsy by Dr. J. H. Wright, March 19, 1902. Each kidney had two ureters and two pelves. The pelvis draining the inferior half of the left kidney was somewhat larger than that draining the superior

Fig. 1.

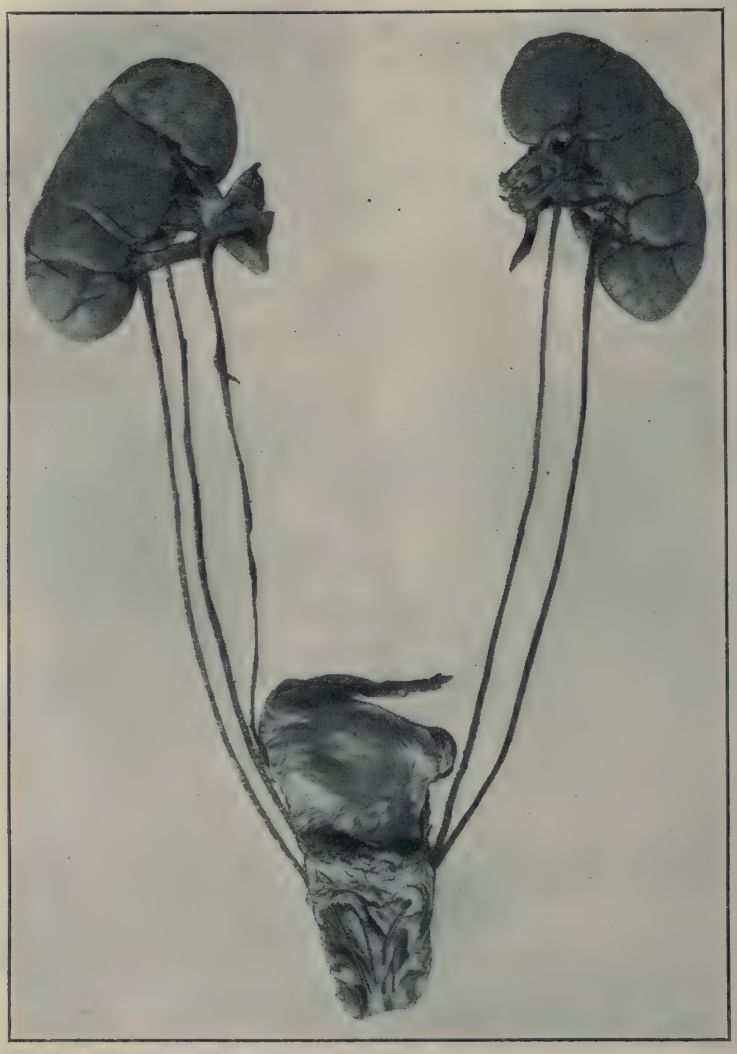


Case I.—Complete duplication of both ureters. (Photograph by L. S. Brown, Clinico-pathological Laboratory, Massachusetts General Hospital.)

half. The pelves of the other kidney were of about equal size. All of the pelves were somewhat smaller than normal. The two ureters of each kidney were separate and patent throughout, and each had its own orifice in the bladder. All four ureters were of equal size and of a diameter somewhat smaller than normal. The orifices of the ureters of the right kidney were situated near, but apparently above, the situation of the normal right ureteral orifice, and were about 7 mm. apart. The ureter from the inferior half of the right kidney had its orifice further from the median line. The orifices of the ureters of the left kidney were about 2 cm. apart. The orifice of the ureter which drained the inferior half of the left kidney was situated apparently a little above the situation of the normal ureteral orifice, while the orifice of the

ureter draining the superior half of the left kidney was nearer the prostatic urethra.

FIG. 2.



CASE II —Complete duplication of both ureters. (Photograph by L. S. Brown, Clinico-pathological Laboratory, Massachusetts General Hospital.)

The right ovarian vein emptied into a large branch of the renal vein instead of into the vena cava. No special anomaly of the main renal artery was noted. The kidneys were 12½ and 13 cm. long, respectively.

The references to the eight cases found in the literature are as follows:

P. Rayer. Traité des Maladies des Reins, Paris, 1837.
Juetting (Double Bladder). Inaug. Diss., Berlin, 1838.
De Font-Réaulx. Bull. Société Anatom. de Paris, 1865, 2d Serie, T. x. p. 645.
Coëyne. Bull. Société Anatom. de Paris, 1868, 2d Serie, T. xiii. p. 55.
Bachhammer (two cases). Archiv. f. Anatomie und Physiologie, 1879, p. 139.
William Ewart. Transactions of the Pathological Society of London, 1880, vol. xxxi. p. 188.
T. C. Janeway. New York Medical Record, March 29, 1902.

APHASIA IN ACUTE DISEASE, WITH REPORT OF A CASE COMPLICATING SMALLPOX.

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Aphasia may occur as a temporary symptom in the course of any one of the acute specific febrile infections, in the puerperal state,[1] in diabetes, Bright's disease, and gout,[2, 3] without there being any evidence whatever of gross organic cerebral lesion. These aphasias are undoubtedly due to the toxins engendered by the specific bacilli operating directly and violently upon the cells of the cortex concerned in the production of articulate speech. Its occurrence has been noticed in typhoid fever by Silvio,[4] Da Costa,[5] Samuels,[6] Billet,[7] and Lopriore.[8] Hutinel[9] asserts that aphasia in typhoid always occurs in children, and most frequently in boys. This statement is true in the main, but since Billet[10] observed its occurrence 6 times in 152 typhoidal soldiers, it follows that it is not infrequently met with in the adult. Silvio believes it to be due to the toxic effects of the typhoidal poison.

This idea seems rational in view of the case related by Van der Kolk,[11] of the gunner in the Dutch Indies who was bitten by a serpent called by the natives "oeloer," and who became completely aphasic, although perfectly conscious until death, four and one-half hours later; and the interesting observations of Wiliam Ogle,[12] who shows that loss of speech may precede loss of consciousness by hours, and even remain absent for some time in event of recovery.

Aphasia has also been found to complicate acute pneumonia, wherein actual lesion of the brain was not made apparent by any other symptom. Osler[13] states that transient aphasia has been met with in a few instances as a complication of pneumonia, setting in abruptly with or without hemiplegia.

Boysson,[14] Carrien,[15] and Rondot[16] have reported cases of aphasia complicating pneumonia.

Aphasia occurring in the course of typhus fever, smallpox, measles, and yellow fever has been obseved by Kühn,[17] Longuet,[18] and Clarus.[19] Boisseau[20] also remarks its occurrence in intermittent fever. Numerous cases have been reported complicating influenza; in fact, cases of almost every kind of acute infectious disease have been recorded in which this complication occurred.

Arnaud,[21] Combemale,[22] Saint-Philippe,[23] and Meyers and Whipham[24] reported disturbances of speech occurring in smallpox.

Combemale states that paralytic disturbances of speech as a complication of smallpox are not uncommon, but he believes that true verbal ataxia is rare.

The following case of aphasia occurring in an otherwise uncomplicated case of smallpox in a boy, aged seven years, is considered worthy of record:

In the spring of 1900 I was called to see E. M., male, white, at 1307 St. Clair Street, this city. The child was found to have a temperature of 103.5° F., some coryza, a slight diarrhœa, and had vomited. It was thought by his parents that his stomach was disturbed by eating a large amount of candy the day preceding my visit. There was no history of exposure to any acute infectious disease, and the case was judged to be a gastro-intestinal disturbance, and treated accordingly.

I was called out of the city the following day, and in answer to a hurried call from the family Dr. F. Y. Allen visited the patient and found the child in violent convulsions, in which he remained for nearly one hour. On the following day I called to see the patient, and found a temperature of 103.5° F., slight rigidity of the neck, child stuporous, breathing regularly, face flushed, and coated tongue. The reflexes were normal; pupils equal and active; no Kernig's sign. Careful examination revealed no rash upon the body, nor did a thorough physical examination reveal other signs of disease. It was thought that he was in a state of meningismus due to gastro-intestinal infection. He remained in this state, paying no attention to anything whatever, and with a temperature that ranged from 103° to 105° F., until the morning of the fourth day, when the characteristic eruption of smallpox became manifest on the calves of the legs and face. The eruption was discrete, frank, and classical. The temperature immediately fell, and the child became conscious, when it was discovered that he was completely aphasic. A very slight secondary fever developed, and the patient made an uninterrupted recovery. At my request the case was visited by the Health Officer, Dr. Friedrich, who confirmed the diagnosis, quarantined, and vaccinated the other members of the family. No other case developed in the family. After the fall of temperature and disappearance of the severe prodromal symptoms the aphasia remained as before, and for a period of over three months the boy never spoke a single word. He seemed to have forgotten all the language he had ever learned. His hearing was perfect, the movement of his tongue, palate, and vocal cords were also normal, but he had to be retaught speech. He seemed to learn readily enough, and in the course of six months was speaking with almost as much fluency as before. It was impossible, for obvious reasons, to properly classify his aphasia, but it certainly was not motor.

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4. Silvio. Raccogli med. forti., 1899, iv. p. 117.
5. Da Costa. New Orleans Medical and Surgical Journal, December, 1899.
6. Samuels. Journal of the Alumni Association, College Physicians and Surgeons, Baltimore, October, 1900.

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11. Van der Koik; quoted by Bastian. Aphasia and Other Speech Defects, 1898, p. 118.
12. Ogle. St. George's Hospital Reports, 1868, p. 167.
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16. Rondot. Contribution à l'étude des paralysies consécutive la pneumonie. Gaz. hebd. des Sc. méd., Bordeaux, 1882.
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19. Clarus. Jahrbuch für Kinderheilkunde, 1874, p. 369.
20. Boisseau. Gazette Hebdomadaire de Médecine, 1671, p. 717.
21. Arnaud. Troubles de la Parole consécutifs à la Variole. Marseille Méd., 1896, xxxiii. pp. 129–140.
22. Combemale. Archives gén. de Méd., June, 1892.
23. Saint-Philippe. Quoted by Combemale.
24. Meyers and Whipham. Lancet, London, March 20, 1886, p. 562.

THE CLINICAL VALUE OF BLOOD PRESSURE DETERMINATIONS AS A GUIDE TO STIMULATION IN SICK CHILDREN.

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(From the Clinical Department of the Thomas Wilson Sanitarium for Sick Children.)

Within a comparatively recent date in the history of medicine several new instruments have been successively brought into more or less general use in the profession for the purpose of representing in numerical terms the degree of various symptoms and conditions indicative of certain morbid processes. Most of these instruments, though at first received with skepticism, have become indispensable to careful diagnosis and intelligent treatment. For example, no one at the present day would question the value of an accurate means of estimating the temperature, the hæmoglobin index, or the leucocyte count; and the thermometer, hæmoglobinometer, and blood counter have become essential aids to every clinician.

During the last few years another means has been introduced into clinical medicine whereby a more accurate idea of a patient's condition may be gained by the use of one or other of the various instruments devised for measuring the actual arterial blood pressure in the circulatory system. Previously in noting the condition, from time to time, during a severe illness or during operative or traumatic states of lowered vitality, a careful observation on the strength of the pulse could only result in an opinion expressed as rather better or decidedly worse, or in some other more or less vague phraseology. That any very

accurate idea of variations in pulse force could be gained from hour to hour, or day to day, even with the most favorably palpable pulse, on such indefinite data as unmeasurable mental impressions, would appear scarcely within the limits of possibility. With many individuals and in many morbid states, especially as met with in pediatrics, the palpation character of the pulse is remarkably deceptive as an indication of actual force, and it is universally recognized, again with special reference to children, how little reliance may be placed upon pulse rate alone.

Mention need only be made of the recent work of Cushing,[1] Crile,[2] Riva-Rocci,[3] Basch,[4] Howell,[5] Erlanger,[6] Brush,[7] Janeway,[8] Gumprecht,[9] Robinowitz,[10] Babajew-Babajan,[11] Carter,[12] Potain,[13] Rosen,[14] Mosso,[15] Hürthle,[16] von Czyhlarz,[17] Federn,[18] Hill,[19] Gärtner,[20] Hensen,[21] Roncoroni,[22] Orlandi,[23] Gottlieb,[24] Kocher,[25] Ekren,[26] Longworth,[27] Shaw,[28] among others to show the increasing importance that this new field is assuming in clinical medicine.

During last summer, as assistant resident in the Thomas Wilson Sanitarium for Sick Children, I was able to appreciate how difficult it is to regulate stimulation in infants and young children by any of the signs ordinarily observed, such as pulse rate and character, temperature, or general condition.

Each case that reached the stage where the necessity for stimulation was apparent constantly presented the two-horned dilemma, whether, on the one hand, if a stated stimulant was ordered at regular intervals, would not the child at some time become over-stimulated; or whether, on the other hand, if stimulation were omitted or lessened, was not the danger of holding off beyond the safety point with resulting collapse imminent. In other words, it was a difficult problem to so regulate stimulation as to keep the child in fairly good stable condition.

In such cases routine blood pressure determinations were made in the hope of obtaining in this way a more accurate criterion for the choice and administration of stimulants.

I have to express my thanks and appreciation to Dr. J. H. M. Knox, physician-in-charge of the Sanitarium, for the opportunity of making these observations, and to Dr. Gordon Wilson and Dr. John Dunlop, assistant residents, for allowing me to follow cases in their charge as well as assisting me in the routine determinations.

The instrument* I used and found most satisfactory is a modifica-

* The instrument is described more fully in an article by Dr. John B. Briggs and the author, to be published shortly.

The manometer is entirely of glass and compact, the better to avoid injury. The upright, tube is best in a solid piece for hospital use, but when it is wished to carry the instrument from place to place, it is convenient to have the long tube in two pieces with a glass joint at the centre so that it may be packed into small compass.

tion I made of the instrument which Dr. Cushing introduced into use at the Johns Hopkins Hospital two years ago, and which was itself a modification of the original Riva-Rocci sphygmomanometer, then in use at the clinic in Pavia.

To Dr. Cushing I wish to express my gratitude for first interesting me in the subject of blood pressure, and for his kind encouragement in work along that line.

The principle of this instrument is a continuous system of air so arranged that equal pressure can be transmitted from a rubber bulb held by the operator to a band placed around an arm or leg of the patient and at the same time connecting with a mercury manometer which registers the pressure in millimetres. In this way the operator can, by a valvular arrangement in the bulb, gradually increase the pressure throughout the air system, raising simultaneously the mercury column and constricting the arm or leg. Keeping a finger on the pulse of the patient's limb on which the constricting band is placed and distal to the band, the operator can read off on the manometer scale the height of the mercury column at the moment the pulse is lost. Just at that moment such a pressure is being applied to the artery under the band that approximates the systolic pressure in the arterial system. Hensen estimates the error due to transmission of the pressure through the arm tissues at not more than 3 mm. in children and 10 or 15 mm. in adults. Usually the momentum of the column of mercury will carry it somewhat above the exact point, but letting it fall slowly back to the point where the pulse returns will confirm the first reading. This may be repeated once or twice without letting the air out, and only varying the column through about 5 mm. until a point is found above which the pulse is lost and below which it returns. This point then is what we speak of as the blood pressure reading. It will usually, except in the most favorable cases, not be more definite than within 3 mm., which about represents the limits of accuracy of the instrument.

The instrument is so easy of application that anyone at all trained in pulse palpation can obtain a fairly accurate estimate after a few minutes of explanation, usually at the first trial. An ordinary observation takes less time than the minute required for an accurate pulse count, and much less time than a temperature determination.

In adjusting the band care should be taken that it is well above the condyles of the humerus, as near midway as possible on the upper arm being the best in children. Should the arm-piece slip over the condyles the reading would be inaccurate on account of the mechanical difficulty in compressing the artery as it lies in the groove between them. The pressure should not be kept up longer than is necessary to obtain a reading, although I never saw any injurious effects of the pressure,

except in one child slight skin ecchymosis on the forearm, which soon disappeared.

All of the determinations spoken of here are those of the maximum arterial blood pressure, which is the best index of the pulse force. Readings of the minimum pressure in favorable cases may be made with this instrument in the manner described by Gumprecht, though the limits of accuracy are between 5 and 15 mm. To obtain the minimum pressure the height of the mercury column is varied until the point is found at which the highest excursions of the column occur during systole after the tube leading to the rubber bulb is clamped off. Usually the minimum pressure is about three-fourths of the maximum, and variations in maximum pressure as a rule are accompanied by parallel variations in minimum pressure.

In recording observations I invariably made use of the graphic chart method, after Cushing, and the pulse rate was noted with each blood pressure reading. When the stimulant effects of drugs was being observed, in so far as was possible, the observations were made at short intervals for some time before the drug was given and until its effect ceased.

The cases stimulated included marasmus, pneumonia, rachitis, pertussis, tuberculosis, and summer diarrhœa, principally the latter. The general clinical side of these cases is soon to be published by Dr. J. H. M. Knox in an article on the "Etiology of Summer Diarrhœa," by Messrs. Duval and Bassett in the *Journal of Experimental Medicine*. These gentlemen isolated the Shiga bacillus from the stools of a large proportion of these summer diarrhœas admitted to the Sanitarium during the season.

As a preliminary guide to stimulation, blood pressure determinations were made on a number of cases where no need of stimulation was apparent—normal children and convalescents—in order to obtain some idea as to what would constitute a normal for different ages.

This normal varies through rather wide limits on account of many factors, including height, weight, and size of arm, and, although we can say such a pressure is good for a child of that age or that another is low, still, in great part, each case must be judged on its own merits, and, by following the blood pressure under changes in treatment, attempt to maintain the one at which the child does best. The value of blood pressure determinations in these cases is not so much an indication for the inauguration of stimulation as it is a guide to the intelligent regulation of the stimulant. On the other hand, routine blood pressure determinations on sick children will often by a low reading give the first intimation that a stimulant would be of benefit or, by a high reading, that the contemplated stimulation could with propriety be omitted. In several cases that were being stimulated on

a two or three-hour order I found the pressure far above a figure at which the child should be able to do well, and, in fact, did as well or better with much less stimulation. Yet without some accurate guide, such as knowing the arterial pressure was remaining constant at a safe level, the stimulant could only be lessened with the fear of ensuing collapse.

In other cases where urgent stimulation was needed and where, after one-half to one hour the blood pressure showed no response to the ordinary dosage, it was repeated again and again at much shorter intervals and in larger doses than could have been safely done without an accurate guide as to the effect it was having. In this way I believe several cases were tided over a temporary depression that probably would have resulted fatally without the extraordinary measures which were warranted by the continued low pressure.

However, in stimulation as in any other form of treatment, we must keep in mind that any one symptom or sign is but a part of the symptom-complex, and that in any case, acting on the indication of a part without considering the whole is illogical and almost certain to lead to errors of judgment; but it seems equally clear that the administration of a class of drugs acting largely on the mechanism of circulation will tend the more to be correct for admitting into consideration the actual arterial blood pressure.

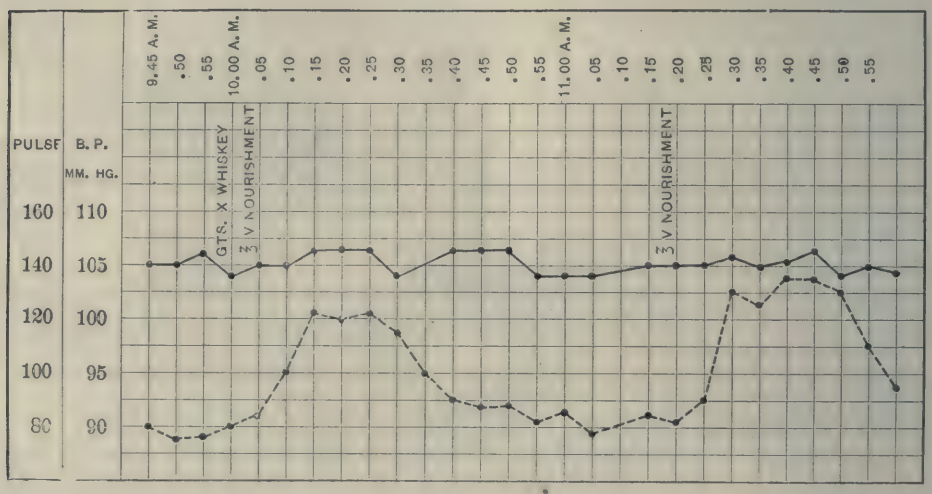
By observations on over fifty cases, at the time in no need of stimulation, an idea could be arrived at roughly as to comfortable limits of pressure for different ages. During the first few months the pressure averages about 70 or 75 mm., and during the last half of the first year, 80 or 85 mm.; but lower than 60 mm. is rare except where the need for stimulation is urgent. During the second year a pressure from 80 to 90 mm. may be expected, and in the third year the range is between 90 and 100 mm., and does not go much above 110 mm. during childhood.

The blood pressure of children is a much more absolute quantity than in adults, when such factors as difference in musculature and arterio-sclerosis make great variations. Children from three to ten years, in health, lying at rest, have a blood pressure that seldom varies within wider limits than from 95 to 115 mm., and for any child between these ages, 85 mm. could be considered moderately low, 75 mm. low, and 65 mm. very low.

The pressure, if nothing untoward or unusual occurred to the child, was found to run very equally from day to day, variations under the same conditions not often being greater than 5 mm. of mercury. Some physiological variations before being recognized as such were rather confusing. For example, in following the pressure of an infant that had been given ten drops of whiskey experimentally, I found

a rise in pressure of 12 mm. in fifteen minutes, and without taking special notice that the infant had its bottle of five ounces of milk five minutes after the whiskey, I was inclined at first thought to attribute the rise to the stimulant effect of the alcohol; but following the pressure for an hour and a half until the next nourishment, I found a similar rise without the whiskey. (See Chart 1.) Repeated observations on this point brought out the fact that after a bottle of five to eight ounces, a physiological rise in blood pressure of from 5 to 10 mm. or more might be expected. This would seem to be very similar to the rise in blood pressure that Crile, Cushing, and others have shown would follow any abdominal compression and inversely comparable to the fall in blood pressure which I have repeatedly observed post-partum or after an abdominal tapping. From a

CHART 1.



Physiological rise in blood pressure after feeding. Infant, aged ten months.

physiological point of view, it is interesting to note in this connection that Hermann, Sigmund-Mayer, and Prinzbram have shown in animals that merely filling the stomach with non-irritating fluids, such as water, may cause a rise in blood pressure. Crying, restlessness, or any manifestation of excitement will also often be accompanied by a rise in blood pressure of 5 or 10 mm. in a healthy child.

These factors, however, seldom interfere in cases requiring stimulation, as they can but infrequently take large quantities of food, and are usually too weak to cry strongly or persistently; indeed, in these weakened and toxic conditions there seems to be a lack of ability on the part of the vasomotor system to respond conformably to such physiological reactions.

A blood pressure chart followed every few hours for several days in the case of a very ill infant, sometimes makes certain more or less

definite curves corresponding apparently to periods of depression and improvement. During the early morning hours, from 3 to 4 o'clock until 6 or 7 o'clock, there may be a fall in blood pressure which rises again toward evening, the period of highest pressure being from 4 to 7 o'clock. This variation corresponds to other well-known clinical phenomena, such as the evening rise in temperature in many toxic cases, and the fall in temperature, the general depression, and frequency of deaths which occur during the early morning hours, which indicate that the early evening corresponds to the period of greatest and the early morning to the period of least resistance.

Observations were then conducted upon cases receiving routine or occasional orders for stimulation in order to find more exactly what effect each drug was having upon the systemic blood pressure.

The routine stimulants were alcohol, strychnine, and digitalin, and occasionally atropine. As a rule, hypodermic administration of the strychnine, digitalin, and atropine was found most satisfactory, as the action was more prompt and certain, and amounts could be better judged than where vomiting, spilling, and larger dilutions had to be taken into account. Alcohol was usually given by the mouth, well diluted, either as brandy or whiskey, and varied or alternated as seemed least to disturb the stomach. Occasionally the whiskey or brandy was given per rectum with coffee or nutrient enemata.

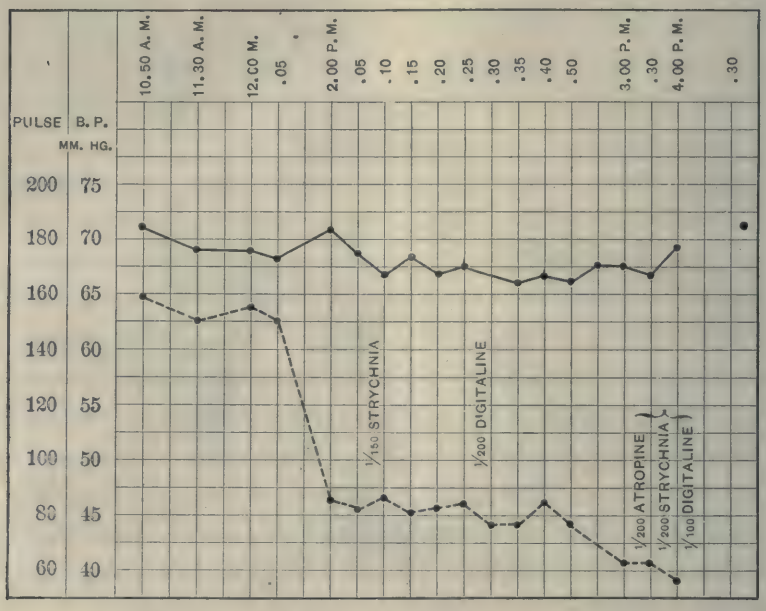
Strychnine and digitalin were usually given in equal dosages, $\frac{1}{400}$ grain to infants over one month and under fourteen to sixteen months. But $\frac{1}{200}$ grain is not excessive and was sometimes necessary in order to produce an appreciable effect, especially in desperate cases. For infants of two years, $\frac{1}{200}$ grain is usually necessary to be effective. The response to strychnine was usually indicated by a rise in blood pressure in from ten to twenty minutes. The rise varied considerably in different cases, usually as much as 10 mm., occasionally as high as 20 or 30 mm. The time during which the rise was maintained also varied greatly, apparently in great part dependent on the child's condition, becoming shorter and shorter as the child became more profoundly toxic and exhausted, six to eight hours being an excellent reaction time; and no rise at all or a rise maintained but for a few minutes, in a number of cases was followed by death in less than twenty-four hours. (See Chart 2.)

Digitalin in equal doses seems to have a more immediate action than strychnine, rather more sure, and causes a higher rise in blood-pressure, which, however, is maintained for a shorter time. The action usually begins in from five to ten minutes, may reach as high as 40 mm., and lasts from one to three hours. (See Chart 3.)

The effects of alcohol for individual doses were not uniform; sometimes a brief rise in blood pressure followed quickly, at others no change

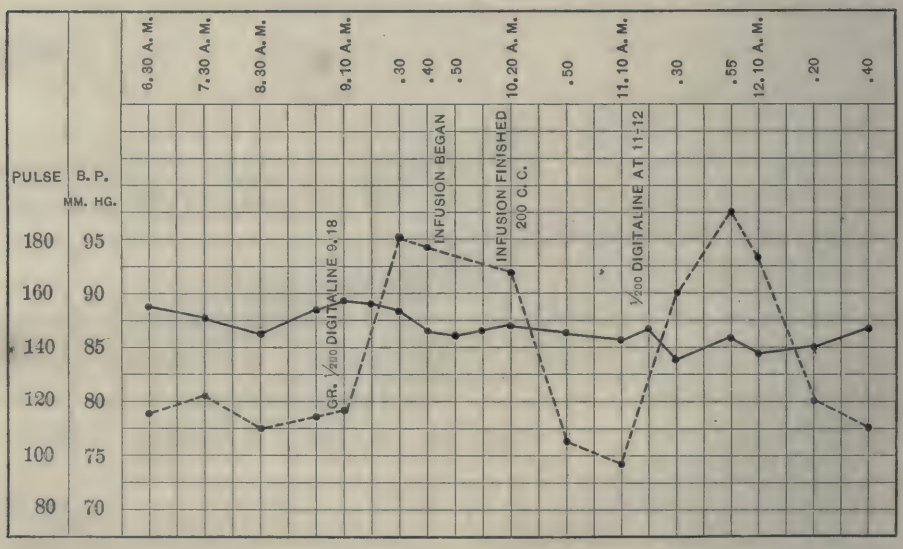
was apparent, and in a few cases a slight fall in blood pressure followed its administration. Many cases, however, showed a gradual, steady, and well-maintained rise in blood pressure under repeated doses of alcohol; and at the same time evidenced improvement by general

CHART 2.



Lethal case, showing no response to stimulation. Infant, aged six months. ● = Died.

CHART 3.



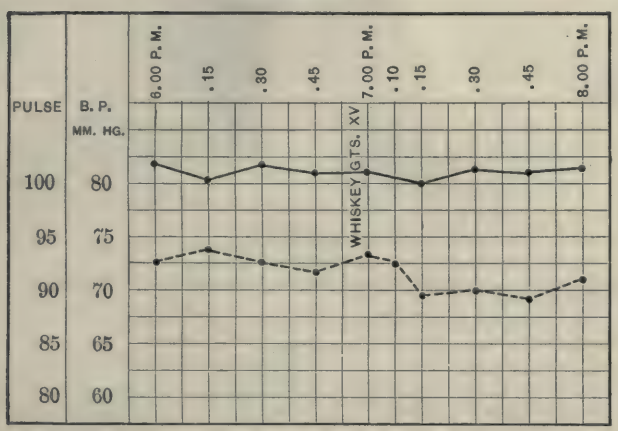
Two rises in blood pressure from digitalin. Infusion negative. Infant, aged eighteen months. Pneumonia.

symptoms, so that the best effects from alcohol would appear to be the result of repeated doses rather than that of any individual dose. (See Charts 4 and 8.) Where the demand for a stimulant is only moderate

it would seem best to start with alcohol in doses of from five to thirty drops, according to the age of the infant, given well diluted and repeated every two, three, or four hours, as seems indicated. Besides what stimulant action alcohol may have, it is a food and acts advantageously as a conserver of energy, even where its stimulant effect is not apparent. The administration of alcohol thus seems the treatment of choice in the more or less slow toxic and marantic conditions in children, and if care is taken to avoid over-stimulation or upsetting the stomach, a child can scarcely take too much.

This form of stimulation may be all that is necessary, but many cases that do not improve, sooner or later reach a stage where a more positive and active stimulant is needed, and other cases cannot for one reason or another take alcohol. It is here that strychnine is of great value in doses of $\frac{1}{400}$ to $\frac{1}{200}$ grain, repeated as infrequently as the maintenance of a safe blood pressure will allow. If the heart becomes

CHART 4.



Negative effect from whiskey. Infant, aged eight months.

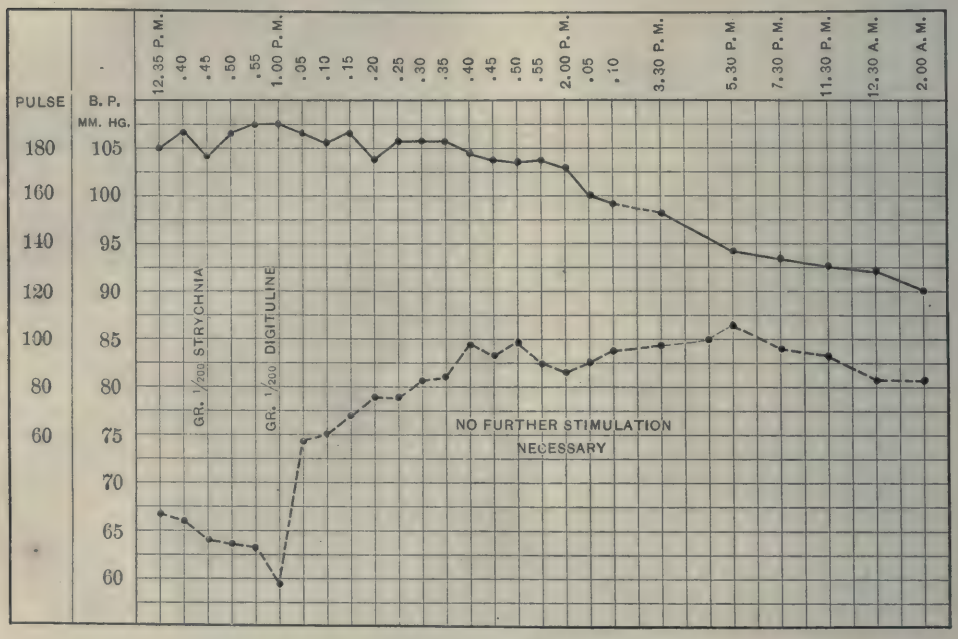
irregular or very rapid, digitalin in the same dosage may be added to advantage; and occasionally during a course of stimulation where the blood pressure is persistently low, digitalin may raise it where strychnine fails.

We may give alcohol until the earliest sign of over-stimulation, a high blood pressure, warns us, but we should conserve strychnine and digitalin so as to give the least amount consistent with the required stimulation. Alcohol is a food, the others at best drugs, and the more unnecessary drugging a child is spared the better for it, though this should not make one skeptical of their value when needed as stimulants. It was in answering these questions of when and how much that I found blood pressure observation so useful.

In sudden turns for the worse during the course of a disease, in threatened collapse, in acute prostration or other rapidly developing

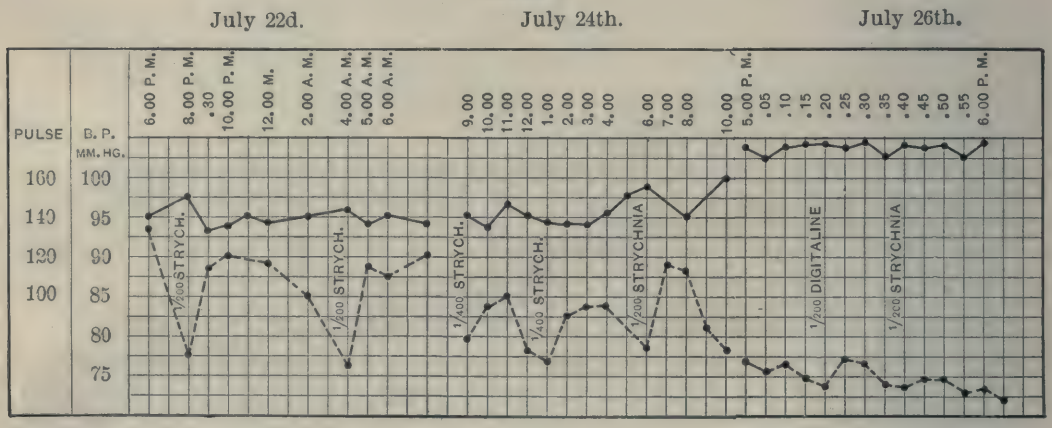
conditions of lowered vitality, always accompanied by low blood pressure, digitalin is the drug of choice, followed by strychnine. (See Chart 5.) Digitalin, $\frac{1}{200}$ of a grain, perhaps repeated, will sometimes bring back an infant apparently on the verge of dissolution, and is best followed by strychnine, which maintains the bettered condition and

CHART 5.



Response to digitalin and strychnine in acute prostration. Infant, aged five months.

CHART 6.



Showing decreasing length and extent of response to strychnine as condition became worse. Infant, aged two years. Died in eight hours.

rise in blood pressure longer than digitalin alone; or both may be given in the same hypodermic. When the blood pressure was near normal and no need of stimulation apparent, the administration of strychnine and digitalin often produced little or no effect on the

pressure; but with a low blood pressure and evident need for stimulation, a very brief rise or no rise at all in blood pressure after sufficient doses of digitalin and strychnine seemed to justify a very bad prognosis. (See Chart 6.) In many cases this lack of response to stimulants, as evidenced by an unchanged or continually falling blood pressure level, gave the first indication of the imminent dissolution.

As digitalin raises a low blood pressure so promptly at first sight, it would seem contraindicated by a high pressure, yet to make this sweeping statement, and on the authority of blood pressure reading, is to take from digitalin one of its chief values and to throw blood pressure observations into disrepute with those whose clinical experience has taught them better. It is merely an example of an unwarranted interpretation to put upon a blood pressure determination. Digitalin, and also strychnine, though apparently to a less extent and less definitely, are cardiac tonics and are indicated in cases of rapid, irregular pulse, in spite of the fact that the blood pressure may be high. Such a condition so aptly expressed as "delirium cordis," where the heart is doing such an amount of work as an abnormally raised blood pressure would indicate, points, though apparently paradoxically, to the use of a cardiac stimulant. In this case digitalin does not raise the blood pressure, but, in steadying a heart which is doing unnecessary work, acts as a conserver of energy in a manner we may speak of as potential stimulation.

The beneficial and quieting effect of a cold sponge in marantic deliriums, such as the post-typhoid, is a parallel illustration of the fact that a stimulant may act as a sedative. In the same way that the stimulus of cold water, which wakens and braces the ordinary sleepy person, puts the delirious convalescent asleep, so does the true cardiac stimulant raise a depressed blood pressure and lower the pressure abnormally heightened by a delirious heart.

Atropine was not often used, but seemed beneficial in some cases, especially those with respiratory distress. It may be found a useful stimulant in selected cases. Besides drugs, other methods in general practice aiming at stimulation were tried.

Following current opinion, infusions of normal salt solution were frequently used, with indefinite results. In no case apparently was the blood pressure more than very transiently raised. Many cases showed after insertion of the needle a temporary rise, which sometimes remained as long as there was local tension at the place of infusion. This was only shown in the least desperate cases, whereas in the cases most in need of stimulation there was no reaction even to the needle puncture, and in some of these cases there was a slight fall in blood pressure.

I think there is no doubt that many cases were benefited markedly

by infusion, either through assisting the elimination of toxins or by supplying to the tissues fluid that could not be obtained in other ways, but I have found little that indicates a true stimulating effect for infusion aside from the local irritation. To infuse a child during a sudden prostration or collapse for the purpose of stimulation would seem useless, in fact worse than useless, for the pain of the puncture and tension would merely be an additional drain upon the vitality.

In cases of collapse with marked cyanosis, a hot mustard bath seemed occasionally beneficial, and is worth trying. Rubbing in hot whiskey or brandy appeared to assist some cases and, with hot-water bags, was used as routine when peripheral circulation seemed poor.

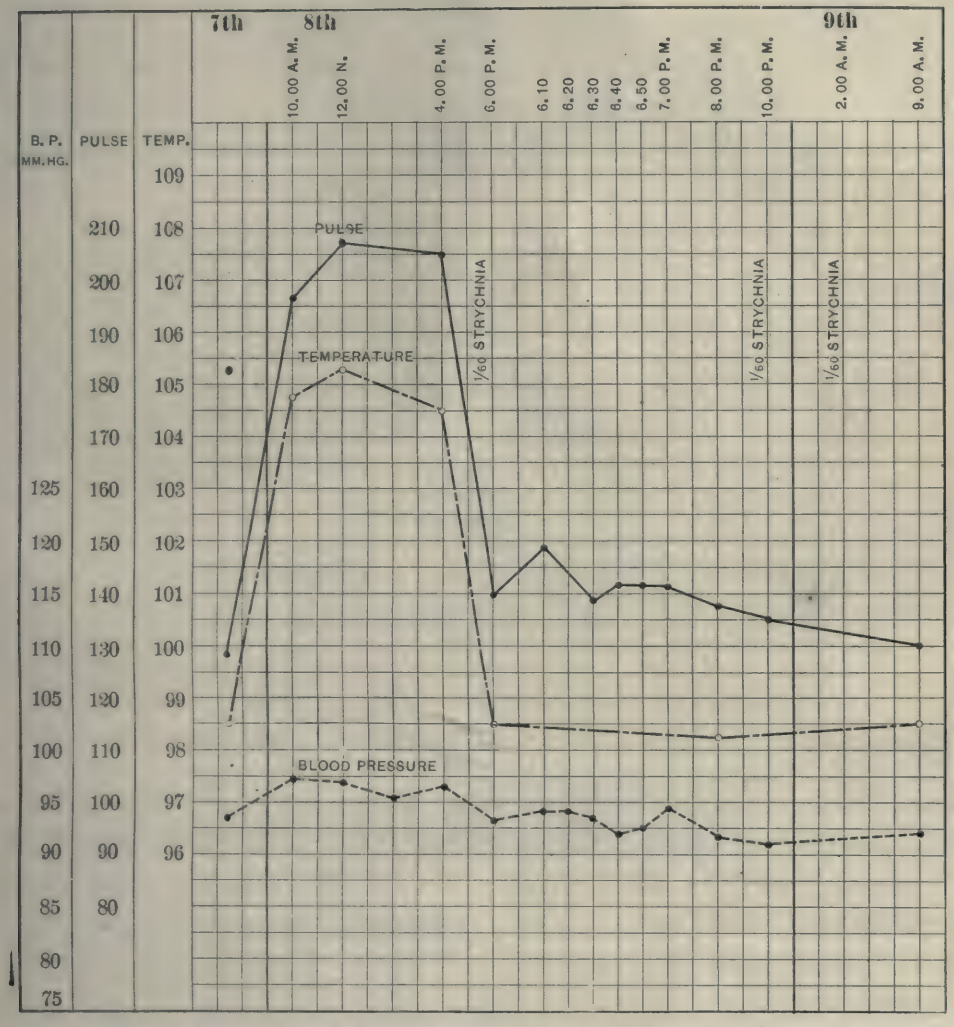
After making blood pressure observations on these cases in order to observe the actual effect of stimulation, the next step was to regulate the amount and period of stimulation by variations in blood pressure, and it was soon found that by occasional observations, say two every two or three hours in ordinary cases, the drug could easily be so given as to maintain a more or less constant blood pressure. To follow a case in this way, keeping at the bedside a graphic picture of systemic vitality in the form of a blood pressure chart, gives a feeling of security in regard to the correctness of stimulation that is a contrast to the uncertainty and obscurity of stimulating on pulse character or general symptoms. This can better be appreciated by citing an example. Suppose the case of a child two years of age, under a certain course of stimulation was doing well and had a full, strong pulse. At this time a blood pressure reading of 95 mm. would agree with the general clinical symptoms and give no indication of any change in treatment, and might appear to be useless if we disregard the great satisfaction it is to know that at any rate we are not giving too much stimulant.

So far the ordinary symptoms have guided correctly, but this child eight or ten hours later may be found dangerously collapsed, so that it may be impossible to restore it even by extraordinary stimulation. If found so the pressure would probably be 40 or 50 mm., and would again agree with the general symptoms in indicating stimulation. But suppose the blood pressure had been taken every now and then in the interval and the decline in pressure had been registered in millimetres, there would then have been an evident need for stimulation long before such a need could be evidenced by the ordinary symptoms. By sufficient addition to the stimulant to maintain the pressure, the danger cited might have been avoided.

Again, to take the converse where unnecessary drugging may be spared a child, such a case is illustrated by Chart 7, a case seen outside the Sanitarium. The pressure had ranged 93 or 94 mm. when in normal condition. The child then underwent an operation,

and twelve hours afterward the pulse went up to 208 and the temperature to 106° F., and when seen had been so for three hours. The pressure had not risen or fallen 3 millimetres. The physician in charge, on the indication afforded by the character of the pulse, ordered $\frac{1}{60}$ grain strychnine every four hours up to three doses. Owing to some delay the first dose was not given for an hour, and by that time the pulse and temperature had fallen to normal. The blood pressure

CHART 7.



Showing relative stability and reliability of temperature and pulse rate in comparison to blood pressure as an indication for stimulation. Child, aged three years. ● = Operation.

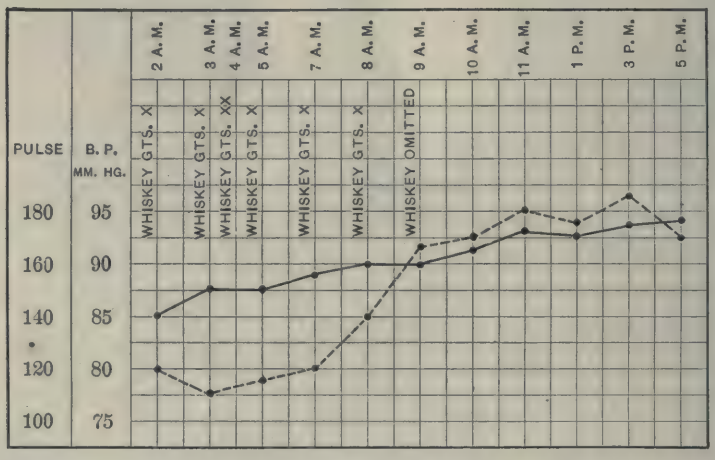
remained constant throughout. Had the order been conditional on changes in blood pressure, the child would have been spared $\frac{1}{20}$ grain strychnine. Children are subject from comparatively trivial causes to such sudden rises in temperature and pulse rate, yet a pulse of 208 at a pressure of 90 mm. feels rather running and thready, and, without the assurance that any actual change in arterial tension would be met

by treatment, many would feel uneasy at leaving such a case without a stimulant.

It was especially at night that I appreciated the value of blood pressure observations, which were taken regularly every one, two, or three hours, according to the severity of the case, by the night nurse, and the child stimulated according to orders given with reference to blood pressure. In the absence of this guide it was not infrequent to be called, and, by the time the child was reached, to find it in collapse, or else to visit the ward in the morning and find the child flushed, restless, and having a bounding over-stimulated pulse.

With stimulants and directions ordered according to blood pressure I believe many such accidents were avoided. This is an example of such an order. For instance, the child had been running a pressure

CHART 8.



Repeated doses of alcohol seem to cause rise in blood pressure. Infant, aged eighteen months.

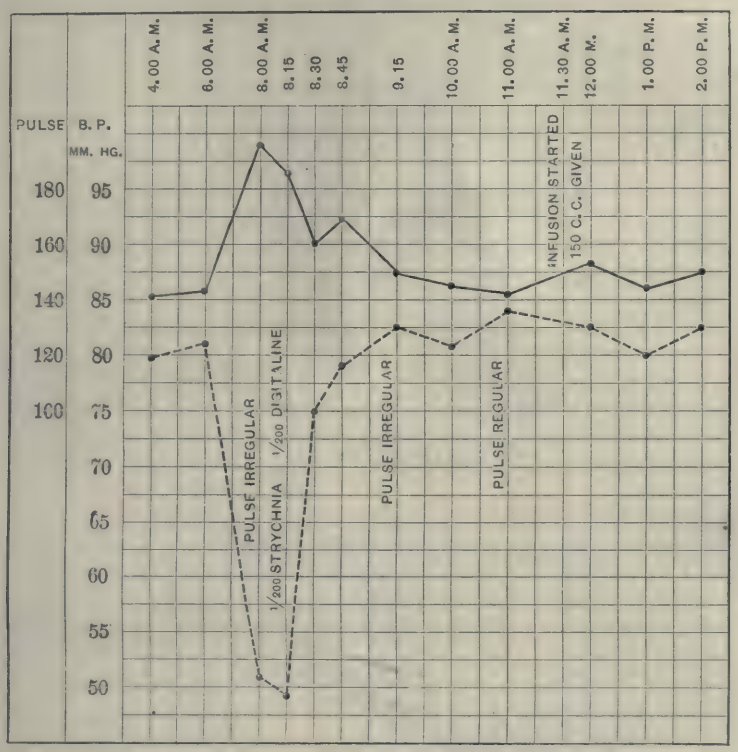
around 95 mm. on an every two-hour stimulation with alcohol alone. The pressure was taken every two hours before the alcohol was given. The order was: If the pressure falls to 80 mm., give $\frac{1}{200}$ grain strychnine; if to 70 mm., $\frac{1}{200}$ grain strychnine and $\frac{1}{200}$ grain digitalin; if to 60 mm., call the physician; if above 105 mm., omit the dose of alcohol.

In hospitals and in private practice where a trained nurse is employed there is no reason why a blood pressure chart should not be kept as well as one for temperature and pulse in those cases where stimulation is or may become necessary. On the morning visit to the ward or home the physician would certainly be in a better position to change or continue his stimulation if he were shown an every two-hour blood pressure chart than if he merely had the patient's present condition and such indefinite data on the pulse character as the nurse might note from time to time to judge from. Even without a nurse

and the advantages of continuous observation, a daily or semi-daily determination by the physician would give another accurate guide for treatment in addition to his more general impression.

From the results of stimulation in toxic conditions in children I do not feel justified in drawing conclusions that similar effects would occur in other conditions of circulatory depression, such as hemorrhage, surgical shock, nor in adult morbid states, as the erroneous impressions of the clinical action of drugs as derived from physiological experiments tend to make one cautious in prophesying for stimulants similar action in different morbid states or in the same morbid state

CHART 9.



Response to strychnine and digitalin in collapse.

under different conditions, without carefully observing each by itself. It would seem, however, that in formulating correct judgments of drugs, especially stimulants, blood pressure observations will be found of great value, as they afford a trustworthy numerical basis from which to work. Observations on blood pressure following these lines are now being made by Dr. J. B. Briggs and the author in the wards in the Johns Hopkins Hospital, and will be reported later.

To my knowledge this was the first time stimulation has been clinically followed and regulated with reference to blood pressure determinations, and the results make me hope that this method may be found of value by others.

I wish again to insist, however, that it is not meant that blood pressure observations, in any form of treatment, should take the place of other signs and symptoms, but merely that an accurate estimation of arterial tension furnishes an additional and not invaluble aid to stimulant therapy.

A certain blood pressure reading is no absolute indication of a patient's condition, but I do believe that variations in blood pressure numerically determined constitute the best single guide to the intelligent administration of stimulants.

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MALARIAL FEVER IN TEXAS: THE FINANCIAL LOSS ARISING FROM THE DISEASE, AND ITS PREVENTION.

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At the present time in Texas the majority of the people are not afraid of malarial fever or its consequences, and in the rural districts, where the disease is more frequently found than in the cities, malarial fever seldom receives serious consideration. A few doses of calomel

and quinine may be administered, which stops the chills temporarily, but any recurrence of it a few weeks later is casually attributed to the drinking water or from breathing "miasm," and is thus looked upon as a fresh invasion.

If one member of a family is stricken down with the disease, and it is transmitted to another member of the family, the origin of the second case is attributed to the same supposed causes as the first one, and so the disease is perpetuated.

It is in those instances where the pallid face and protruding belly caused by an enlarged spleen, or the congestive type of the disease, becomes apparent that much active interest is shown.

The conditions necessary for the perpetuation of malarial fever in Texas might be said to be most excellent. It should be noted especially that before many years from this time a very large part of the extreme southeastern and southern portions of the State will be turned over to the cultivation of rice, and thus large areas will be covered entirely by water. Water for rice irrigation stands on the ground for several weeks, and frequently from the middle of June to the end of August, or during a period when malarial fever may be said to be quite active.

That the malarial carrying mosquito—Anopheles—may be found in these localities, I can state positively, for during a trip of several months' duration in southeastern Texas (Jefferson County) last summer, I found no less than three different species of Anopheles abounding, and no less than four breeding-grounds for them within a radius of one square mile.

In Louisiana (which adjoins Texas) there are thirteen different localities where rice canals are maintained and capable of flooding 211,320 acres of land, or an area of 330 square miles.

In Texas developments along this line have just begun, and, besides several huge rice canals to be built, there are many rice canals, distributed in different localities, and capable of irrigating 150,000 acres of land, or an area of 135 square miles. Five localities are: Terry, Trinity, Beaumont, Orange, and Port Arthur.

Up to this time I have been able to obtain Anopheles in three different sections of Texas, as follows: (1) Central Texas, at Waco; (2) East Texas, at Tyler; and (3) Southeast Texas, at Beaumont.

Three different species of Anopheles have been found, namely: (1) *Anopheles quadrimaculata* or *claviger* (at Tyler and Beaumont); (2) *Anopheles punctipennis* (at Waco, Tyler, and Beaumont); and (3) *Anopheles crucians* (at Beaumont and Tyler).

Having spent several months in and around Beaumont, in Southeast Texas, during the summer of last year, I had exceptional facilities for studying conditions regarding malarial fever there, and I shall speak at some length regarding this section of Texas.

Beaumont is a rapidly growing city of 17,000 people, situated on the west bank of the Neches River, in Jefferson County, or in the extreme southeastern portion of Texas. The Neches River at Beaumont is a stream of water probably 300 to 400 feet wide.

Beaumont is situated in a level country, and the business and dwelling-houses extend directly to the river's bank. On this west bank of the river, while there is an unbroken prairie country on the opposite side, there is an extremely dense forest, and a thick undergrowth of palmettos and high grass. The forest country on the east bank, being more or less flat, is subject to overflows from the river, and is thus frequently under water.

Toward the west, northwest, and north of Beaumont lies a level unbroken prairie for many miles. The land is very black in color, with a clay subsoil. In certain localities extensive marshes may be found, and after a heavy rainfall these marshes or "dug-outs" are capable of holding water for weeks and even months. I have found Anopheles breeding in these marshes.

During June and July the mosquitoes in the city of Beaumont were most annoying, and myriads of them could be seen collected in dark corners and out-of-the-way places in hotels, water-closets, and vacant store-rooms. I examined hundreds of these, but found that there was not one Anopheles. All were *Culex*. I have no doubt, however, that a more thorough search in the suburbs would have revealed Anopheles.

Some time later, while on a fishing expedition some three miles east of Beaumont (Orange County, Texas), I had occasion at night to sleep in a mining camp situated in a dense forest. In this camp there were about eight or ten employés, most of whom had been suffering from a severe form of dysentery, probably due to filthy drinking water. With one or two exceptions, all the members of this camp slept entirely unprotected from the bites of mosquitoes, and none had suffered from chills because the Anopheles had probably not become infected. On several successive mornings in the tents I had no trouble in catching female Anopheles quadrimaculata. These Anopheles were, therefore, caught in a dense forest; but I also caught them in houses situated in the open prairie country, six or seven miles from any timbered land.

July, 1901, I spent mostly in the central portion of Jefferson County, Texas, and near a small railroad village of three or four houses. This railroad station is situated on an open prairie, which is so level that after heavy rains the water in shallow depressions or "dug-outs" remains on the ground for weeks or until evaporation occurs. Toward the west about one mile there is a dense forest.

It is essentially a rice country, and is fast becoming converted into the cultivation of this product, for which artificial irrigation is necessary. Many rice farms have what are known as "reservoirs," capable

of holding large quantities of water, and kept for the purpose of overflowing the land periodically. Around the edges of these reservoirs I found algæ growing, and during July I searched many of them carefully, but never found a single specimen of Anopheles larvæ. In some of these marshes, however, I found myriads of Culex larvæ. In this connection it must be noted that during the summer months there are thousands of aquatic birds (snipe, coot, crane, duck, killdee) which swarm around these ponds, and thus in a measure limit the number of mosquito larvæ.

During August, 1901, and while penning these notes, I made a search of the room for adult Anopheles, and on looking over the ceiling and walls, usually in the dark corners, succeeded in catching nine Anopheles, six of which were quadrimaculata (claviger) and three crucians. Culex were also present in the same rooms, but, strange to say, Anopheles were almost as abundant as Culex.

While residing around this locality I had the opportunity of seeing several cases of malarial fever.

About one-fourth of a mile north of this station I found two breeding places for Anopheles. The pools were formed by backwater in a marsh which extended along a railroad embankment.

In Philadelphia I found a similar breeding pool for Anopheles along a railroad embankment. So far I have heard of no law in any State compelling railroads to either limit or to drain these pools along their line of travel.

In this connection it might be noted that, as a rule, the Anopheles does not fly far for its food—probably not over one mile—therefore, it would not be unjust to compel railroads to drain these pools of water at least within a limited distance from cities and towns.

In another pool of water some four or five hundred yards west of the former ones noted, I found another breeding ground for Anopheles. It was located in a marsh which had been recently flooded by a heavy rain. In this pool no algæ was growing, and the larvæ seemed to exist entirely on the green leaves of weeds or grass which extended out into the water for some distance.

A few weeks later, and about one mile north of these breeding-grounds, I for the first time caught the larvæ of Anopheles growing in small receptacles around an inhabited house. This time I found them in large quantities in a barrel containing a few gallons of rain-water and a few dead leaves. Culex were also present with the Anopheles larvæ.

In several of the fresh-water pools in which Anopheles larvæ have been found I have also seen fish (pike and perch) swimming about, and in fact, have watched them both thus living and developing together in small pools of water for over three months, so that for this and other

reasons, I have come to place small reliance on fish as a means of exterminating Anopheles.

Probably one of the most frequent questions asked one who holds that infection in malarial fever occurs through the bite of an *infected* Anopheles is " how can it be explained that malarial fever occurs during the winter months when there are no mosquitoes and in those regions where mosquitoes do not abound."

For the latitude of Philadelphia, at least, I think I have been able to prove[2] that mosquitoes do live throughout the entire winter. It cannot be gainsaid, however, that malarial fever does occur during the cold, winter months, and sometimes manifests itself immediately after the breaking up of extremely cold weather when the ground has been covered with snow and ice. While in Philadelphia I thus saw a case which had developed after a severe blizzard. In this instance for several days previous to the onset of the chills the weather had been quite warm, or like spring, with cold nights and warm days. The history of this case may be detailed as follows:

T. C., aged fourteen years, a patient of Dr. A. H. Davisson, had come to the Out-patient Department of the Children's Hospital of Philadelphia, on February 27, 1901, giving a history that two years previously he had lived in Delaware County, Pennsylvania, and during June and July had suffered from chills, occurring every two days, followed by fever, and continuing for about one week. His younger brother living in the same house was also similarly affected at that time. In June or July of 1900 (year previous) he again had chills, coming on about 11 A.M., and followed by fever lasting two or three hours. For this attack he took quinine for about one week, after which he felt perfectly well. During the winter he was employed in a large dry goods house in Philadelphia, and remained in good health until February 20, 1901, when he had a hard, shaking chill at 11 A.M., which recurred two days later, and was followed by fever and sweats. On February 27th the blood was selected, and stained with eosin and methylene blue. One group of tertian parasites almost full grown were found. The pigment was scattered throughout the body of the parasites in very fine granules.

The second case occurred during the past winter in Texas, and, as in the first case, previous to the onset the weather had greatly moderated after a severe freeze, and the atmosphere was like that of spring, with warm days and cool nights. The history was as follows:

Patient, Mrs. E. H., aged forty-six years, had recently come to Texas from Tennessee. She stated that in July of the previous year she had suffered from a chill each day for several successive days. She took a few doses of quinine, and the chills then recurred every two days, disappearing at the end of one week. At this time two of her children also suffered with chills and fevers. Patient felt well during the winter until February 20, 1902, when she had a shaking chill at 3 P.M., followed by fever and sweats. A second chill occurred two days after the first one, and still another chill two days later. At this time the blood was selected, and stained with carbol-thionin. A double

tertian infection was evident, there being more than one group of pigmented parasites present. The parasites were abundant, sometimes as many as four of them being present in one microscopic field.

In these two cases I believe the evidence points toward the attacks of malarial fever during the previous year as the initial invasions, while the occurrences during February were relapses. The two cases demonstrate too clearly the inefficacy of a few doses of quinine in permanently eradicating the disease.

The latter case is most interesting in many respects. It emphasizes: (1) the highly infectious nature of the disease, since she stated that two of her children had also been afflicted at the same time in the previous year; (2) the carelessness displayed by the patient in continuing the quinine treatment; (3) the refractive power of the malarial parasite against the specific action of quinine; (4) the tendency of the disease to relapse; and (5) the history of the case explains how easy it would be for a patient to have chills and fevers in regions where there were no mosquitoes. In my opinion, this patient was never cured of malarial fever in Tennessee, but harbored the malarial parasites in the blood all during the winter, finally bringing them with her to Texas, when, upon the advent of warm weather, she became attacked by an increased number of the same parasites. It is also interesting to note that shortly after the mother's attack in February of this year her two children also began to have chills and fevers, which came on every two days.

As to the question regarding the existence of malarial fever in localities where there are no mosquitoes, one cannot be positive in saying that "where there are no Anopheles there is no malarial fever," since this latter case illustrates how the disease may be transported for over a thousand miles. One might, however, be safe in saying that "where there are no Anopheles there are no autochthonous cases of malarial fever."

Malarial fever might occur in the Arctic zone without the aid of mosquitoes.

One thing is known—that every person whose blood contains malarial parasites does not necessarily have fever or chills. In fact, it has been calculated[3] that at least 250,000,000 malarial parasites must be present in the blood of the patient in order to bring on an attack of fever and chills.

Just how long the parasites may lie dormant in the system without producing untoward symptoms is not known. One case has been spoken of in which malarial parasites had been dormant for two years, and upon the patient taking violent exercise (mountain-climbing in a foreign country) a recurrence of the disease came on. On examining the blood the same type of parasite was found as those two years previously.

We sometimes hear of regions in which there are said to be no mosquitoes. This claim might, perhaps, be proved for a limited number of sections during certain periods of the winter months. Such claims might be set forth by promoters in the interest of health resorts to catch the incredulous, but must be accepted by scientists with a very great deal of hesitancy. Frequently I have been told by families in which malarial fever was prevailing that they had not been bothered by mosquitoes, but on going into the house and making a search have found Anopheles filled with blood hanging on the ceiling or walls of the sleeping-rooms. I have repeatedly had patients to tell me they could feel nothing, although at the time I could see an Anopheles lay hold and fill herself with blood.

Koch has claimed[4] that malarial fever is more prevalent among children than among adults. For instance, in one village in mid Java he found that adults remained apparently healthy, but among 86 children examined 9.2 per cent. showed malarial parasites. In another locality, of 141 children examined 12 per cent. were malarious, while in still another region, of 189 examined 22.8 per cent. were malarious. He, therefore, declared "that by examining the blood of children an absolutely trustworthy knowledge of the prevalence of malaria in a given community may be determined."

Since young children, as a rule, do not have shaking chills the disease may pass on into the congestive form before its real nature is disclosed. In the case of children, therefore, the therapeutic or "quinine test" becomes most unreliable as a diagnostic measure in disclosing the disease.

Statistics regarding the different types of malarial fever prevailing in Texas are most incomplete, for the reason that here it is uncommon in general practice to make a diagnosis of the disease by a microscopic examination of the blood. Probably the most accurate statistics regarding this question may be obtained from the John Sealy Hospital of Galveston (Department of Medicine, University of Texas), where a microscopic examination of the blood is more frequently resorted to than in many other institutions. For three years past[7] the report is as follows:

Year 1899.		Year 1900.		Year 1901.	
Tertian malarial fever,	64 %	Tertian malarial fever,	82 %	Tertian malarial fever,	40 %
Quotidian "	4 "	Æstivo-autumnal "	9 "	Æstivo-autumnal "	54 "
Æstivo-autumnal "	10 "	Pernicious "	2 "	Pernicious "	1 "
Pernicious "	6 "	(hemorrhagic) "	1 "	Chronic "	4 "
Chronic "	14 "	Chronic "	3 "		
Total number deaths,	3	Total number deaths,	4	Total deaths, none.	

At the hospital of the St. Louis Southwestern Railway, of Tyler, Texas, no absolute records are kept in regard to the type of malarial fever admitted, but an estimate based on clinical evidence alone is about as follows: tertian chills, 66.66 per cent.; quotidian chills, 16.66 per cent.; quartan chills, 1 per cent. to 5 per cent.; irregular type and seven-day chills, 8 per cent.

STATISTICS OF MALARIAL FEVER AS OBSERVED IN ONE HOSPITAL OF EAST TEXAS. (HOSPITAL OF ST. LOUIS SOUTHWESTERN RAILWAY, LOCATED AT TYLER, TEXAS.)

	Total number of patients treated in hospital.	Number of cases of malarial fever.	Percentage of patients affected by malarial fever.
Year ending June 30, 1896	2279	1424	62 %
" " " 1897	1739	816	47 "
" " " 1898	1701	994	58 "
" " " 1899	2362	1303	55 "
" " " 1900	1686	951	56 "
" " " 1901	1588	815	51 "
	11,355	6303	General average 55 %

Number of deaths from malarial fever from June 30, 1896, to June 30, 1901, were 3.

It may be interesting to note in connection with this last-named hospital that during the year from 1896 to 1897 a total of probably over 26 pounds of quinine were given to patients for malarial fever and other diseases, without ever having produced a single case of hæmoglobinuria or hæmaturia; and, further, that of the 5 cases of hæmoglobinuria treated from 1893 to 1896 inclusive, all took quinine, and all recovered.

On account of the fact that at this time Texas has no State Board of Health, and keeps no correct data in regard to vital statistics (!), and on account of the fact that malarial fever heretofore has not received the attention which it is destined to receive, there has been no effort on the part of the cities in the State to determine its prevalence, therefore the absolutely correct financial loss to Texas from malarial fever at this time cannot be learned.

In this paper I have made an attempt to estimate this loss, by selecting the records as preserved in at least nine different localities of the State as follows: (1) The statistics from the hospital of the St. Louis Southwestern Railway in East and including Central Texas, which receives patients covering a distance of about 300 miles; and (2) the statistics from the seven different army posts in Texas, which are located all along the western border of the State, a distance of 600 miles. Statistics from the John Sealy Hospital, at Galveston, represent only the percentage of cases treated in the wards of the hospital, and not the percentage of population for the whole city of Galveston.

STATISTICS OF MALARIAL FEVER AS OBSERVED IN THE HOSPITAL, DEPARTMENT OF MEDICINE, UNIVERSITY OF TEXAS (JOHN SEALY HOSPITAL OF GALVESTON, TEXAS). (SOUTH TEXAS.[6])

Year 1899.	Year 1900.	Year 1901.
1. Total number of patients treated in the wards of hospital, 1645.	1. Total number of patients treated in the wards of hospital, 1738.	1. Total number of patients treated in the wards of hospital, 1115.
2. Total number of cases of malarial fever, 141.	2. Total number of cases of malarial fever, 193.	2. Total number of cases of malarial fever, 72.
3. Percentage of patients affected with malarial fever, 1 to every 12.	3. Percentage of patients affected with malarial fever, 1 to every 9.	3. Percentage of patients affected with malarial fever, 1 to every 15.

The hospital of the St. Louis Southwestern Railway receives patients from points all along the entire line of the road from Texarkana, in the extreme northeastern portion of the State, to Gatesville, in Central Texas, a distance of nearly 300 miles. The total number of employés on this road in Texas during the year ending June 30, 1901, was 1661, and the total number of cases of malarial fever brought into the hospital was 375, or 22 per cent., or 1 case of malarial fever to every 5 employés.

The total number of employés on this road during the year 1901 for the States of Missouri, Arkansas, and Texas was about 3996. For Arkansas and Missouri, 2335, and for Texas, 1661. The total number of cases of malarial fever from Missouri, Arkansas, and Texas during this year was 815, or 20 per cent. of all employés. During the year 1900 the number of employés being about the same (3996), the total number of cases of malarial fever brought to the hospital was 1303, or 32 per cent. of all employés.

It should be noted that these figures are only for those employés brought into the hospital. Probably half as many were treated by local surgeons at different stations all along the route of the road.

According to these statistics, the total number of employés (general average 26 per cent.) incapacitated for the previous six years would have been 9342. If a day's labor is valued at $1.50, and each patient lost on an average ten days from work on account of sickness from malarial fever, the total financial loss to the employés of this railroad would have amounted to $23,335 annually, or a grand total for six years (1896 to 1901 inclusive) of $140,000.

Statistics of Malarial Fever as Observed in Seven Different Army Posts in Texas (West Texas).

Northwest Texas. Fort Bliss.	Extreme Southwest Texas. Fort Brown.	Southwest Texas. Fort Clark.	Southwest Texas. Camp at Eagle Pass.	Southwest Texas. Fort McIntosh.	Southwest Texas. Fort Ringgold.	Central Southwest Texas. Fort Sam Houston.
In El Paso, El Paso County.	Brownville, Cameron County.	Bracketville, Kinney County.	Eagle Pass, Maverick County.	Laredo, Webb County.	Rio Grande City, Starr County.	San Antonio, Bexar County.
1. Mean strength of fort for twelve years (1885–1897), 1928.	1. Mean strength of fort for twelve years (1885–1897), 1394.	1. Mean strength of fort for twelve years (1885–1897), 5217.	1. Mean strength of fort for eleven years (1886–1897), 681.	1. Mean strength of fort for twelve years (1885–1897), 1897.	1. Mean strength of fort for twelve years (1885–1897), 1850.	1. Mean strength of fort for twelve years (1885–1897), 6235.
2. Total number cases malarial fever, 236; percentage affected, 1 to every 8 persons.	2. Total number cases malarial fever, 849; percentage affected, 1 to every 2 persons.	2. Total number cases malarial fever, 758; percentage affected, 1 to every 7 persons.	2. Total number cases malarial fever, 107; percentage affected, 1 to every 6 persons.	2. Total number cases malarial fever, 141; percentage affected, 1 to every 13 persons.	2. Total number cases malarial fever, 214; percentage affected, 1 to every 8 persons.	2. Total number cases malarial fever, 716; percentage affected, 1 to every 8 persons.
3. Average loss of time from active service, seven days.	3. Average loss of time from active service, four days.	3. Average loss of time from active service, seventeen days.	3. Average loss of time from active service, nine days.	3. Average loss of time from active service, fifteen days.	3. Average loss of time from active service, fifteen days.	3. Average loss of time from active service, eleven days.
4. Number of deaths from malarial fever, none.	4. Number of deaths from malarial fever, one.	4. Number of deaths from malarial fever, four.	4. Number of deaths from malarial fever, none.	4. Number of deaths from malarial fever, three.	4. Number of deaths from malarial fever, none.	4. Number of deaths from malarial fever, none.

According to these statistics from the seven different army posts in Texas, the results show that during the twelve years from 1885 to 1897, the average number of soldiers affected by malarial fever was 1 to every 7 persons; and further, that in the seven different army posts the average loss of time from active service on account of malarial fever was eleven days. The total number of deaths for the twelve years from malarial fever was eight.

In the United States army posts in Texas the percentage of soldiers affected by malarial fever for twelve years (1885 to 1897) was 1 person to every 7; at the hospital of the St. Louis Southwestern Railway, 1 to every 5. Taking these nine (except John Sealy Hospital) localities as a guide to the prevalence of malarial fever throughout the entire State of Texas, it is found that 1 person to every 6 falls ill of malarial fever.

Personally I believe that these statistics throughout Texas do not represent the true proportion of cases of malarial fever, and that they are too high because the diagnoses were for the most part based on faulty methods—clinical symptoms. One may perhaps come nearer the true status of the condition by dividing the number of cases into one-half. For the nine districts cited, the average person affected by malarial fever in Texas would then be 1 to every 12!

Estimating, therefore, that each person afflicted (1 in 12) loses on an average of ten days from sickness, and valuing a day's labor at $1.50, and considering the population of the State to be 3,200,000 (census of 1900 gave it over 3,200,000), it is found that the financial loss (estimating that each patient pays in medical fees $5.00) to the people amounts each year to the enormous sum of $5,333,320!

In order to prevent malarial fever in any community, it is first necessary that one should start out by upsetting the ancient ideas regarding the manner in which the disease is contracted. Ronald Ross, working in India and Africa, proved that malarial fever was contracted through the bite of an infected mosquito—Anopheles. Later, Marchiafava and Bignami, in Italy, and Koch, in Africa, confirmed the discovery of Ross; and still later, Thayer and myself, in America, and Guiteras, in Cuba, confirmed the work of Ross.

It thus appears that up to this time the burden of proof rests upon those who hold to the opinion that infection in malarial fever occurs through other avenues than through the bite of an infected Anopheles. Until that time does come it should be the aim of everyone to lessen the danger from this disease by fighting against at least one known agent.

At this time it can be safely said that the malarial parasite does not propagate itself in lowlands, marshes, or swamps; that a moist and hot climate does not favor the development of the malarial parasite *per se;* that the malarial parasite does not breed either in the soil or in the water of marshes; that it is impossible to contract malarial fever through the inspired air. As stated by Ross, "*It is the malarial carrying mosquito* and *not the malarial parasite that flies through the air.*" The proposition stated in a positive sense would be that malarial fever in man can be contracted in only one way (so far discovered), and that is through the bite of an infected Anopheles. All else is theory.

It appears that man himself acts as the sole intermediate host in the life history of the malarial fever (the mosquito in this sense acting as the definitive host).

It has not yet been established that the malarial parasite of the lower animals can be communicated to man. Therefore, to get rid of human malarial fever it is only necessary to destroy the parasite in the blood of man.

Koch selected[8] the lower animal which he thought most nearly akin to man—the ape (hylobates agilis and hylobates syndactylus)—and by injections of blood from a case of tertian malarial fever, endeavored to transmit malarial fever to them, but none of them contracted the disease.

The inoculability of the disease having been fully established, the question of prevention can be considered with better prospect for its eradication. In other words, the task devolves upon the State or municipality to purge its domain of this easily preventable disease. Being a preventable and highly inoculable disease, boards of health should make it compulsory on the part of physicians to report all cases of malarial fever. If necessary, appropriations should be made to combat the disease in each county throughout the United States. In New York City an appropriation of $10,000 has been asked for this purpose, and to be employed in that municipality.

The laity must be educated so that each person who has malarial fever will fully understand just how he becomes a menace to his neighbor, and who by this means will not readily rebel against the restrictions imposed upon him.

Health officers should insist that all instructions given by them be carried out to the letter. Proper penalties should be provided.

There appears to be two direct ways of attacking this disease. Probably the quickest way would be to protect each and every case of malarial fever by means of a closely fitting mosquito netting, especially at night, since the Anopheles seldom bites during the daytime. In this way the malarial carrying mosquito could not become infected and would be harmless. In the case of those who already have the disease the parasites should be attacked by large doses (4 or 5 grains of quinine in hydrochloric acid solution) repeated every three or four hours. Microscopic examination of the blood should be made every week or two, and the quinine continued until all parasites are gone. In this way those cases which now go through the winter and relapses will be prevented. A close surveillance should be kept over new arrivals from districts in which the disease prevails. This duty becomes more apparent in cities near the sea-coasts, in order that fresh importations may be prevented.

Lastly, attempts should be made to destroy as far as possible the

breeding grounds and larvæ of the Anopheles. A thorough system of drainage offers the best promise.

According to my experience, the larvæ of the malarial carrying mosquito may be found only in the outskirts of cities or rural districts, and usually in small slowly flowing streams of fresh water containing algæ or greenish moss.

In order to destroy the larvæ of mosquitoes,[9] I have found by certain experiments, carefully conducted, a strong solution (say 1 pound to 10 gallons) of tobacco in kerosene oil most efficient. This solution may contain the active principles (nicotine and nicotianin—both practically insoluble in water) of tobacco, but whatever it may be, this solution killed mosquito larvæ more quickly than did plain kerosene oil, or kerosene oil containing camphor or naphthalin. This solution is cheap, is practically non-poisonous, and can be obtained everywhere. All substances used for the destruction of these larvæ should be applied once every two or three weeks, and need frequent *agitation* in order that they may spread over a wider area than would otherwise be the case.

By combating the disease with these or better methods, those who come after us in Texas and elsewhere fifty years hence it is to be hoped may view malarial fever with that complacency of security which we at this time look upon yellow fever.

NOTE.—My thanks are tendered Dr. C. A. Smith, Chief Surgeon of the St. Louis Southwestern Railway Hospital, of Tyler, Texas; Dr. Lester Smith, and to the clerk of the hospital, Mr. J. W. Smiley, for statistics.

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5. Compiled from a chart kindly furnished me through the courtesy of Surgeon-General George N. Sternberg, U.S.A., and Assistant Surgeon-General Charles Smart, U.S.A.

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UPON THE ASSOCIATION OF EPILEPSY AND HEART DISEASE.

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(From the Pathological Laboratory of the Ohio Hospital for Epileptics.)

Introduction. From time to time the assertion has been made that heart disease is a cause of epilepsy. As a consequence, the term "cardiac epilepsy" has come into vogue with the implication that this is a form of epilepsy *sui generis*. These claims have been repeated so often of late that a review of the subject, with the addition of any observed facts, will perhaps be of interest, especially in view of the circumstance that no detailed report has been published in this country; indeed, comparatively few papers have appeared in English. Statistics bearing on the frequency of heart disease and epilepsy in combination are not very easily secured. Stintzing[1] claims that 1 per cent. of all his patients with heart disease had epilepsy, and that of 63 epileptics only 2 had heart disease. The *Report of the Craig Colony for Epileptics for 1901* states that of 1050 entrance examinations nearly 8 per cent. had clinically demonstrable valvular lesions, while nearly as many had minor cardiac disturbances, as irregularity, etc. An analysis of the post-mortem records of this hospital does not give quite such high figures. In 190 autopsies we found but 9 valvular lesions, and our experience corresponds with that of Gowers,[2] who thinks that organic heart disease is not more frequent in the subjects of epilepsy than would be expected from its general distribution.

Historical and Critical Review. While, as Mahnert[3] remarks, the literature of cardiac epilepsy is young, it is not inconsiderable. Litre[4] seems to have been the first, in 1834, to have mentioned heart disease and epilepsy in connection, stating that affections of the right heart may sometimes be the cause of seizures in young children. A case in which an improvement in a heart lesion brought about an amelioration of coexisting fits was reported by Delasieuve,[5] in 1852. From this date to the time when Lemoine,[19] in 1887, published the article which has given rise to most of the recent discussion there are scattered references to the subject. It was thought by Lepine[6] that epilepsy might be due to congestion. He based his conclusion upon the improvement obtained from the use of digitalis. Knövenagel[7] claimed to have seen a case in which a patient had epileptic attacks in the course of an acute rheumatism concurrently with signs of insufficiency thought to be due to myocarditis, and disappearing with the recovery of the heart. He admits, however, that the fits were "not quite

typical." Writing in 1893, Gowers[8] thought that fainting attacks due to heart disease sometimes were on the border-line of epilepsy, and no doubt some of them would pass into epilepsy if not relieved. However, in the last edition of his *Epilepsy and Convulsive Diseases* he states that an abnormal condition of the heart is not met with in a sufficient number of cases of epilepsy to indicate a definite relation to the idiopathic disease.

There are also a good many observations as to the connection of arterial disease and epileptic attacks, Balfour[9] stating that all slow pulses, however caused, may result in pseudo-epileptiform or in pseudo-apoplectiform spasms. The English journals contain several references to this subject of slow (infrequent) pulse and epilepsy, as Tyson,[10] Boyce,[11] Gibbings,[12] Bristowe.[13] These authors treat the subject almost entirely from the clinical point of view, and seem to favor the opinion that the bradycardia is in some way responsible for the attacks. However, a case was reported by R. L. Jones[14] where mitral regurgitation and slow pulse coexisted with epileptic attacks, and in which the infrequence of the pulse was thought to have been of neuropathic origin. Hearder[15] reports a case (with autopsy) of aortic regurgitation, with epileptic seizures, and St. George Mivart[16] one in which swoons of the epileptic type came on in a patient with heart disease upon stooping. It was thought by Crocq[17] that vessel changes in the brain might occasion such attacks, and Ballet[18] had seen epileptiform fits in a patient the subject of Graves' disease.

In 1887 Georges Lemoine[19] published an article entitled "De l'Epilepsie de Origin Cardiaque et son Traitment." This author is the most outspoken advocate of epilepsy of cardiac origin, and holds that there are two distinct types of the disease—one due to cerebral congestion and the other to cerebral anæmia. He cites the fact that profound hemorrhages in animals give rise to vertigo, syncope, and sometimes convulsions. Illustrating the cases due to congestion of the brain, Lemoine gives two examples of mitral regurgitation. The first instance had to do with a man, aged thirty-five years, without neuropathic heredity and with no other known exciting cause, who had had heart disease fourteen years and epilepsy for three years. The attacks were, as a rule, brought on by lying down. In the second the sequence was rheumatism, pain in the heart region, mitral regurgitation, and then epileptic attacks, with cardiac aura. In both these cases the attacks improved greatly after the use of digitalis. The third case, which Lemoine thinks proves the existence of cardiac epilepsy due to brain anæmia, occurred in a patient who had symptoms of aortic disease at twelve years, and developed fits, with cardiac aura, beginning in the fifteenth year. Treatment with caffeine brought about great improvement. Lemoine thinks the attacks following heart disease are not quite similar

in all respects to ordinary grand mal, and he maintains that as our knowledge increases we shall have fewer cases of idiopathic epilepsy and more of those with known cause.

The case of a man, aged twenty years, who had first syncopal and then epileptic attacks is reported by Laache.[20] Here the autopsy disclosed chronic endomyocarditis.

Huchard,[21] in 1889, ascribed epileptiform attacks occurring in connection with slow pulse to sclerosis of the vessels of the heart and of the nervous system.

Analyzing a series of 904 epileptics, E. Mendel[22] states that 5.8 per cent. were late epilepsy, by which he means epilepsy of onset after the fortieth year. Among these heart disease preceded the onset of the seizures two or three times; but in another place (*Versammlung der Deutsche Naturforscher*, 1893) he claimed that the two diseases had no connection. In the discussion at this meeting von Leyden concurred with Mendel's views, but Klemperer dissented.

In 1893 Rosin[23] reported a case of myocardial degeneration, in the course of which the patient had, between the forty-ninth and fifty-ninth years, eight attacks indistinguishable from true epilepsy; the last of these seizures was fatal. From a study of this and "about twelve" similar cases the author concluded that this form of epilepsy, depending upon disturbed cerebral circulation and the consequent impairment of nutrition, might be due to any form of heart disease if other causes could be excluded. It occurs, however, most commonly in myocardial degeneration and arterio-sclerosis. An individual predisposition is generally present, this author says, as epilepsy is rather rare in diseases of the heart. Similar to this example of Rosin's is the case of a young man reported by Pritchard.[24] The patient, aged twenty-three years, with marked hereditary neurotic taint, suddenly began to have attacks of palpitation, at first with vertigo, pallor, and transitory unconsciousness; later, grand mal and petit mal developed.

In a discussion on a paper by Luntz[25] dealing with an instance of Adams-Stokes' disease, in which an improvement in the condition of the heart muscle brought about a cessation of the attacks, Kornlow and Butzke claimed that the fits were accidental or syncopal.

Three cases are cited by B. Naunyn,[26] in which he thinks it was clear that the fits were due to cerebral anæmia induced by disease of the vascular system. They were all in old men—two of them with arterio-sclerosis and one with aortic regurgitation and chronic endocarditis. One of these patients had attacks if he sat up suddenly, and in all of them compression of the carotids brought on convulsions. Naunyn tried compression of these arteries in young people, but without other effect than slight vertigo. This agrees with the experience

of Concato,[27] who also found that he could induce seizures in an epileptic, aged sixty years, by compressing the carotids, but that he could not do so in young people. Among the many cases of brain anæmia which have been reported, Naunyn thinks some of them were associated with true epileptic attacks, and cites those of Corkey and Hubbarty, and Luntz. With this last statement Lauterbach[28] agrees. He thought, too, that he could see improvement in an epileptic, aged eighty years, with general arterial sclerosis, when digitalis was given. Tebaldi[29] also held that arterial anæmia and venous congestion were pathognomonic of epilepsy. Mahnert[30] thinks that the causal relation of disease of the heart or vessels to epilepsy is proved by the improvement of the epilepsy with the gain in the condition of the circulatory apparatus. He differs from Lemoine,[31] claiming that such attacks are in all respects similar to true epilepsy. Mahnert gives details concerning three cases of his own—all old men, with marked arterio-sclerosis and heart lesions—each of whom was improved by medication directed to the heart disease. This author discriminates sharply between attacks associated with valvular lesions in young people and those of old people in whom disease of the vessels is also present, and would make for the latter a new class of "senile arterio-sclerotic epilepsy." In the case of those with heart disease only he thinks the attacks are the result of disturbed circulation. For the arterio-sclerotic cases he offers the new and ingenious explanation that the attacks are most common if the small vessels in the brain are affected, and that the paroxysms are caused by injury to the ganglion cells from the impact of the stiffened vessels at each impulse of the heart. In this category C. L. Allen[32] added four cases of epilepsy with senile arterio-sclerosis, and held with those who claim such cases to be the result of heart, *i. e.*, of circulatory, disturbance.

That epileptic seizures may be due to circulatory disease other than valvular lesions or arterio-sclerosis is made probable by the experience of H. Beer[33] and A. Smith,[34] the former reporting an instance of attacks with apparent recovery, due, he thinks, to hypertrophy and dilatation of the heart without valvular lesion or arterio-sclerosis; and the latter thinks he can show that the cardiac dilatation of chronic alcoholism is sometimes the cause of epileptic fits.

In 1899 R. Stintzing[35] reviewed critically the evidence for and against the existence of cardiac epilepsy. He holds that there are several possibilities to be taken into account:

1. Both the epilepsy and heart disease may be the result of the same cause, as syphilis, Basedow's disease, or alcohol. This, however, seems unlikely.

2. One may cause the other (*a*) by itself, or (*b*) with the aid of some other disease. While epilepsy might occasion a temporary dilatation

of the heart, it could hardly cause a genuine heart lesion. On the other hand, it seems not unlikely, *a priori*, that heart disease might cause epilepsy, if we have in mind the common explanation of fits as due to vasomotor disturbances and the fact that late in heart disease convulsions are sometimes present. But in order to establish this causal relation it must be shown (1) that the heart disease precedes the epilepsy; (2) other causes must be excluded; (3) the coincidence must be frequent; (4) an improvement in the heart disease must cause an improvement in the fits. The first and fourth of these conditions seem to be met in many cases. It is, however, never possible to exclude all the causes. The coincidence is not very frequent.

3. They may have no relation to each other.

4. As a rule, epilepsy has but little effect on heart disease, but heart disease may aggravate the epilepsy or give it a peculiar character, as an angina, before or after the attacks. While the author warns us at the beginning of his paper that he will agree with Binswanger[36] that no causal nexus has been established, he seems really to grant that heart disease may be a factor, as he says, in conclusion: "The occurrence of heart disease and epilepsy together is, as a rule, accidental. When they do coexist the heart disease is not the sole cause of the epilepsy, but other factors, as alcoholism, heredity, etc., are also present. Heart disease and arterio-sclerosis may, however, favor the occurrence of epilepsy by causing circulatory disturbances (anæmia of the cortex). Particularly is this true of senile epilepsy."

Senile and cardiovascular epilepsy are discussed by F. Schupfer,[37] who, after a brief report of nine cases, turns to the consideration of the conditions of the vessels of the head during epileptic seizures. While Betcherew (*Neurologisches Centralblatt*, 1895 and 1897) found that during artificially induced fits the pressure in the cerebral arteries and in the cerebro-spinal fluid was increased, other experiments have given such confusing results that we can only say that during epileptic attacks the pressure conditions are very various. But it is not proved that epileptic spasms do not cause anæmia. There are several conditions of the cerebral circulation to be considered: (*a*) Complete ischæmia (tying all four of the cerebral vessels). This, as shown by Tenner and Kussmaul, causes convulsions, which are not, however, typical epilepsy, as they do not run a regular course. Perhaps this fact may throw some light on the irregular forms of attacks. (*b*) Much the same is to be said of passive congestion from ligating the jugular veins. (*c*) Partial ischæmia by closure of the carotids has been shown by several authors to be capable of bringing on an attack, though it failed in Schupfer's hands. Partial ischæmia from thrombosis, etc., within the skull is frequently signalized by convulsions if the plug is not near enough the beginning of the Sylvian artery to cut off transmission by injury to the basal structures. If the

arteries are healthy, only dizziness results when the carotids are compressed; if, however, the heart is weak, it is conceivable that blood enough might not be sent to the middle and anterior portions of the brain, and convulsions would result, but these would be only of the tonic type. If, in addition to the weak heart, the end vessels are sclerotic, compression of the carotids may result in the same signs as in the case of thrombosis of the vessels—*i. e.*, typical fits of the cortical variety. This author thinks that under favorable circumstances severe heart disease may bring about the same conditions as closure of the carotids. There is the further possibility that the pressure which was applied to the carotids may have caused the fits by irritation of the cervical sympathetic or by pressure on an epileptogenic zone. Schupfer concludes that we may have, aside from irregular fits due to vascular disease, typical epileptic spasms when in the presence of heart disease there is sclerosis of both the larger cerebral vessels and their terminal twigs.

The theory that cerebral congestion may have a part in the causation of epileptic seizures is opposed by A. Bier,[38] who says that by placing a rubber band about the neck the venous congestion of the brain may be increased almost at will. That Bier's procedure did really cause congestion was proved by the case of an epileptic with an aperture in his skull, in whom the brain could be made to well up as much when the band was applied as when the patient had a fit. This artificial congestion, tried upon ten epileptics, was found to be borne extremely well by them; indeed, the author thinks that it rather diminished the number of attacks than otherwise. In a discussion of Redlich's[39] paper, in which it was maintained that there is a genuine senile epilepsy aside from that due to symptomatic causes, Schlessinger said that his idea, based on long observation, was that heart disease and epilepsy occurred together only accidentally.

The majority of the authors quoted seem to be more or less definitely committed to the theory of the existence of cardiac epilepsy. The simplicity of Lemoine's view that cardiac epilepsy is solely a question of cerebral anæmia or congestion evidently has not escaped unscathed the criticism of the later writers, and it is extremely doubtful if the matter is by any means so easy of explanation as Lemoine thought it to be. From a general survey of the whole subject it seems plain that Mahnert greatly helped to define the problem by insisting that there were two classes of cases—one occurring in young people with heart lesions, and the other in older ones who have involvement of the vascular system as well (the arterio-sclerotic cases). The instances of the young patients with no other known cause than the valvular affection seem to present the simplest problems, but are, as a matter of fact, the most difficult of explanation. That such valvular heart lesions may very well bring about altered conditions in the cerebral

circulation is reasonable enough, but the connection of such disturbances with epilepsy seems to rest largely upon presumptive evidence. Most of the arguments that refer to disturbances of the circulation apply to both the juvenile and the senile cases, and are based chiefly on clinical grounds. One of the strongest points is the improvement that results from a betterment in the condition of the heart. For the fact that improvement does take place we have the authority of many competent observers (Delasieuve, Lepine, Knövenagel, Lemoine, Luntz, Mahnert, A. Smith, Lauterbach). It will be noted that some of the cases are explained by a reference to disturbed circulation without any attempt at more definite reasoning, as Mahnert, in the simple heart cases; H. Beer, A. Smith, and in Ballet's case of epilepsy in Graves' disease. When the explanation takes a more specific turn we find the authorities divided; Lemoine, Mivart, Lepine, and Kussmaul, ascribing the attacks to congestion, while Schupfer and others take the ground that epileptoid seizures occurring in the course of congestion of the brain are not true epileptic fits, and that when they are caused by experiment they do not run a typical course (Kussmaul and Tenner). Still more extreme is the position taken by A. Bier, that congestion rather diminishes than increases the attacks.

Most effort has, however, been devoted to the attempt to establish a connection between anæmia of the brain and the epileptic attacks. Anæmia might, of course, be the result of some of the heart lesions, as aortic regurgitation, but seems *a priori* to be the condition most likely to occur with arterio-sclerosis. While experimentation has given rather more encouragement here than in the case of congestion, most of the evidence is again clinical. Cutting off the whole blood supply of the brain will cause convulsions, but not true epileptic fits. It is claimed that partial ischæmia will do the same thing, as is proved by the fact that thrombosis in the cerebral arteries is frequently ushered in by convulsions. That this holds true, at least in part, for arterio-sclerotic epilepsy, is shown by the occurrence of fits upon the closure of the carotids in such people (Naunyn, Concato, Kussmaul). To this conclusion is urged the objection that these fits may be due to pressure on the vagus or on an epileptogenic zone, which, as Schupfer points out, may cause spasms. Clinically, it is assumed that conditions causing anæmia have fits as a result (Naunyn, Lemoine, Lauterbach, Schupfer, and the English authors). That this is not always so is shown by the results of ligation of the carotid undertaken as a cure for epilepsy, which seems never to have made the fits any worse.

The questions of congestion and anæmia do not exhaust the possibilities. Cardiovascular disease might cause vasomotor spasm in the brain, though this theory is largely given up; or it might cause

changed pressure in the cerebral arteries (Betcherew), or irritation of the vagus (Carderelli[40]). To these must be added malnutrition of the brain (Lüth,[41] Rosin), and in the case of arterio-sclerotic epilepsy, direct injury to the ganglion cells (Mahnert).

The difficulty of settling on any theory that is at all satisfactory is made manifest by a consideration of the large group of observers who are unable to see any connection at all between the two conditions (Binswanger, Schlessinger, von Leyden, Kornlow, Butzke, Stintzing).

Personal Observations. In our experience at the Ohio Hospital for Epileptics the occurrence of valvular lesions of the heart does not seem to be much more common among epileptics than among others. It seems, as a rule, easy to divide our patients into two classes—those of the juvenile type, with valvular lesions, and those of the senile type, in which there is, in addition to the heart disease, more or less arterio-sclerosis. The cases which follow illustrate the concurrence of heart disease and epilepsy.

I am indebted to Dr. A. P. Ohlmacher, Superintendent of the Ohio Hospital for Epileptics and Director of the Pathological Laboratory, for the autopsy notes which, unless otherwise stated, have been taken from his memoranda. It will be understood that for the sake of brevity the descriptions of organs, or of whole sets of organs, have been frequently omitted without comment when the findings seemed not to bear upon the subject in hand. Besides supplying the post-mortem notes, I have to thank Dr. Ohlmacher for bringing this subject to my notice, and for much assistance.

The following notes are abbreviated from a memorandum by the writer:[42]

Case I.—S. A., female, was admitted to the Ohio Hospital for Epileptics August 20, 1894, when thirty-six years of age. There are several brothers, of whom one is said to be an epileptic. Previous to the first seizure this patient had typhoid fever and inflammatory rheumatism of the lower extremities, and to the latter affection she ascribes the onset of her epilepsy. Since the first attack, five years ago, in the thirty-first year of her age, the epileptic paroxysms have occurred at irregular intervals, averaging about one a month, and from her description seem to have been severe. The patient's attacks, as witnessed since her admission to the hospital, resemble those of idiopathic grand mal, without any aura. These seizures occurred rather irregularly, from one to eight or twelve per month.

During the five years of residence at this hospital the patient was never sick in bed, but had occasional attacks of incompensation, at which times she had œdema, and complained of shortness of breath, but usually recovered in a few days.

Seen April 15, 1899, the following notes were made:

The patient lies propped up in bed, dyspnœic, moderately cyanotic, with cough and bloody expectoration and marked tense œdema of the

feet and slight puffiness of the face. The chest is large and well formed. The apex-beat is not to be seen or felt. There is well-marked heart shock, but no thrill can be felt. The dulness is somewhat enlarged to the left. The lower sternum is quite dull, and the dulness extends high up along the left border of the sternum. On auscultation in the apex region the first sound is extremely loud and sharp. There is a loud, harsh murmur, beginning with the first sound, suddenly becoming quite soft and of different character, and fading away some time before the loud first sound again recurs. The second sound is not heard at the apex. Both sounds are heard at the base; the first pulmonary is louder than the second, and is accompanied by a blowing murmur. The pulse is full, but soft and quite regular. There is moderate dulness, with small, moist râles and blowing breathing low down in the back. The abdomen is level with the ribs; there are no signs of fluid in it, and neither the spleen nor the liver can be felt, although there is tenderness in the region of the latter organ.

The urine is brownish; specific gravity, 1040; and it solidifies upon the addition of nitric acid after boiling. The sediment is copious and made up of large and small casts of all descriptions—hyaline, hyaline with granules, many bearing leucocytes and epithelial cells, and occasionally red blood cells. There are also free leucocytes, epithelial and blood cells in the urine.

Clinical Diagnosis. Mitral regurgitation and stenosis (?); nephritis; epilepsy.

Pathological Résumé. The necropsy was held May 2, 1899, eight hours post-mortem. There is pronounced rigor mortis. The abdomen is somewhat distended, and contains about 100 c.cm. (3 ounces) of clear fluid.

The liver adheres to the diaphragm; it weighs 1910 grammes (63 ounces). On section, a moderate interstitial hepatitis is revealed. The spleen weighs 360 grammes (12 ounces). The kidneys together weigh 290 grammes (9.6 ounces), and present a roughened surface. The capsules adhere, and when pulled off leave a universally broken surface, with reddish depressions and raised, yellowish foci. The cortex is narrowed about one-half, and is mottled yellowish-red. There is bilateral, almost complete obliterating pleuritis, with about 500 c.c. (16 ounces) of clear fluid in each side. In both lungs the lower lobes are pneumonic, being flesh-like, solid, and sinking in water, with a little fluid escaping on section; abundant frothy, blood-stained fluid issues from the cut surfaces of the upper lobes, and similar fluid flows from the mouth as the lungs are squeezed. There is moderate œdema of the glottis. The right lung weighs 860 grammes (29 ounces) and the left 850 grammes (28 ounces). The bronchial glands are large, and some of them contain caseous foci. There is complete obliterating chronic pericarditis, without, however, much pericardial thickening. The heart, which is extremely flabby, weighs with its adherent pericardium 500 grammes (16 ounces). There are a few minute atheromatous spots in the aorta. The coronary arteries are slightly atheromatous, but not obliterated. In the examination of the whole fresh organ it was discovered by palpation that both the mitral and tricuspid orifices were so narrow as to admit only the tip of the index finger, the edges being thickened, rigid, and almost cartilaginous in consistency; but the aortic valves, while somewhat thickened, were movable and proved competent by

the hydrostatic test, and the pulmonary valves were quite unaltered.

The heart was fixed whole in formalin without further dissection. The whole hardened heart, which has preserved its original shape remarkably well, measures 14 cm. (5.7 inches) in length, 9 to 10.5 cm. (4 inches) in width, and 30.5 cm. (12 inches) in circumference. On cutting, all the chambers were much distended, without much hypertrophy of the ventricular walls. The wall of the left ventricle varies in thickness from 14 to 17 mm. (0.5 to 0.6 inches), and that of the right from 5 to 8 mm. (0.2 to 0.3 inches). The pulmonary valves are not thickened. The aortic valves are slightly thickened. There is well-marked stenosis of both the mitral and tricuspid valves, that of the mitral being a little more pronounced. Both project as rigid cones into the ventricles. The mitral opening is irregularly triangular in shape, 17 mm. (0.6 inches) in its greatest length and 13 mm. (0.5 inches) in its greatest width. The tricuspid orifice is roughly pyriform, 16 x 10 mm. (0.6 x 0.4 inches). The papillary muscle, on macroscopic section, shows the usual whitish, irregular scars of fibrous myocarditis. The brain weighs 1290 grammes (43 ounces), is rather soft, but shows no macroscopic lesions.

Pathological Diagnosis. Mitral and tricuspid stenosis and insufficiency, with adherent pericardium; chronic myocarditis; obliterating pleuritis; hydrothorax; lobar pneumonia; chronic interstitial hepatitis; cyanotic induration of the kidneys, and acute nephritis.

The progress of the heart disease does not seem to have had much effect on the frequency of the attacks in this instance, as they continued up to the time of the patient's death to be about as frequent as usual.

CASE II.—F. S., male, aged forty-six years, admitted October 26, 1898. There is said to have been no nervous disease in his family. His epilepsy is of thirteen years' duration. He has been known for some time to be the subject of chronic heart disease, and has exhibited himself to medical classes, having a musical heart murmur. The epileptic attacks are severe. He always falls in a convulsion, frequently injuring himself. The seizures occur at very irregular periods, but are frequent. The patient had several such attacks during his brief hospital residence. He was very violent, being maniacal, with marked homicidal and suicidal propensities. A few days before his death he complained of an ulcerating tooth, and became so irritable that it was necessary to seclude him. He was fed with difficulty, threatening his care-takers. A day or two before his death it was noticed that his abdomen was distended, and he died in collapse.

Urine. The urine from the bladder at autopsy gives a marked albuminous reaction, and the sediment consists of great numbers of large, coarse, granular casts and an abundance of small epithelial (kidney) cells.

Death took place at 4 A.M.; necropsy begun at 8 A.M. same day, December 23, 1898. The abdomen is uniformly distended and tympanitic, and its walls are very tense. The peritoneum is reddened, and there is an exudate of fibrinopurulent flakes and thin, purulent fluid. There are half a dozen ulcers, with ragged edges, and smooth floors in the lower end of the ileum. Large and small ulcers are found in the cæcum, and one of these has perforated.

No adhesions are found in the pleural or pericardial cavities, and

there is no excess of fluid. Both lungs are voluminous; the upper lobes crepitate freely, while the lower lobes are chocolate in color, sodden, and crepitate but slightly. On section, a frothy, chocolate-colored fluid flows freely from the lower lobes. The lungs together weigh 1430 grammes (47.6 ounces).

The heart weighs 380 grammes (12.6 ounces). Its flesh is more pale and flabby than normal. The right posterior sinus of Valsalva has a dense calcareous mass projecting into it, and the segment of this semilunar aortic valve is thickened and somewhat shortened, so as to interfere with the perfect closure of the valvular orifice. A similar small calcareous deposit is present at the base of the anterior mitral segment, and the valve, together with the tendinous chords attached to it, is somewhat thickened. There is a slightly increased thickness of the left ventricular wall and a moderate dilatation of the corresponding cavities. The aorta presents several patches of beginning sclerotic alteration about its cardiac end.

The liver weighed 2050 grammes (68.3 ounces), and contained two rather large gummata. The liver substance is pale and softer than normal.

The kidneys together weigh 285 grammes (9.5 ounces). The cortex is swollen, and the peculiar pallor of the proper cortical substance brings the bloodvessels into marked prominence.

The spleen is swollen and extremely soft. It weighs 480 grammes (16 ounces).

The skull is of average thickness. The subarachnoid fluid is somewhat more abundant than usual. The pia is of a milky opacity, and close inspection shows numerous small, white, opaque areas in this membrane. No other alterations in the brain, and the cord appears unchanged. The weight of the brain is 1350 grammes (45 ounces).

Anatomical Diagnosis. Typhoidal ileocolitis, with perforation of the cæcum; fibrinopurulent peritonitis; cloudy swelling and gumma of the liver; splenic tumor; acute parenchymatous nephritis; chronic aortic endocarditis, with insufficiency; mitral insufficiency (?); hypertrophy and dilatation of the left ventricle.

Bacteriological Analysis. B. coli and streptococcus pyogenes from purulent abdominal exudate; B. typhi in pure culture from the spleen and mesenteric glands.

It is to be noted that this patient had no attacks during the month of December, most likely on account of the presence of the typhoid.

Case III.—J. C., male, aged twenty-five years; admitted October 25, 1898. No history of heredity can be obtained. The patient is one of four children; the others are well. When a child he is said to have had typhoid fever; and at the age of fourteen years, following exposure, he was in bed several weeks with an attack of acute articular rheumatism involving nearly all the joints. The first epileptic attack occurred when the patient was twenty-three years old. The seizures at first were at night, but latterly occurred, as a rule, in the daytime. Those seen at the hospital resemble, in every respect, ordinary grand mal. They are very infrequent. The patient is dull; there seems to have been but little change in the mental condition in the last two years.

The patient says he considers himself (aside from his epilepsy) to be in good health, and does not complain of any symptoms ascribable to

the heart. Physical examination, however, reveals the characteristic signs of aortic insufficiency. The apex-beat is not plainly seen, but is felt as a moderately strong impulse in the sixth intercostal space, a finger's breadth outside the nipple line. There is a striking impulse in the neck, especially in the supraclavicular notch, where a strong impulse is imparted to the finger. No thrill can be made out anywhere. The dulness is moderately enlarged to the left, extending about to the nipple line. There is a slight dulness over the upper part of the sternum. There is a typical murmur, rather loud, blowing, most intense in the third intercostal space on the right, and loudly transmitted down the sternum. It is also faintly heard at the apex. In the suprasternal notch there is a loud, booming first sound and a very faint diastolic murmur. The heart's rhythm is slightly irregular. The radial pulse is rather quick and moderately full. There is no capillary pulse. No further abnormalities can be made out. The urinary examination is negative.

Clinical Diagnosis. Aortic regurgitation; dilatation of aorta(?); epilepsy.

CASE IV.—L. H., female, aged thirty-seven years; admitted November 23, 1899. The father is living. The mother had mild chorea in childhood, but no sequelæ. She died in childbed. There is no other history of nervous disease in the family.

The patient and one of her sisters had chorea in a mild form at the time L. was eight or ten years old. This sister also had epilepsy, and died at about the age of forty years, in a seizure. The patient, who is intelligent, says she had articular rheumatism when she was thirteen. She was sick in bed, but does not remember many details. The attacks began when she was twenty-eight. About the same time there began to be trouble with the heart, consisting in moderate shortness of breath, but chiefly in palpitation and aching pain in the left side and arm, which came on in paroxysms. Now she has attacks which cannot be distinguished from idiopathic grand mal with aura. She becomes short of breath, the heart palpitates, and she seems to hear people talking. They always say the same things, but in the intervals the patient is unable to remember the words. Her sensations during the auras are pleasant. The aura is not always followed by a fit. There have been several times when she was in bed on account of dyspnœa, but she is sure that the attacks were not worse at these times.

The patient is a slight woman, rather undersized. The skin is somewhat pale. There is no œdema. Examination of the heart shows a tremulous impulse in the second, third, and fourth intercostal spaces. The apex-beat is seen below the sixth rib, a finger's breadth outside the mammary line. The impulse is forcible, but no thrill can be felt. The rhythm is subject to great variation. Sometimes there are thirty beats to the quarter of a minute, and in the next quarter but sixteen, without any evident cause for the alteration. There is occasional asystole, generally at the time of the abrupt change in frequency. The absolute dulness reaches the nipple line toward the left, but its area is not enlarged upward or toward the right. At the apex the second sound is faint and the first replaced by a loud, sawing, systolic murmur, with a whistling quality at the end. This bruit is heard all over the heart area except in the region of the aortic valve, where there is also a systolic murmur, but of a different quality from that in the mitral

area. This is not well transmitted upward. The second sound in the pulmonary area is much accentuated. The pulse is small and soft and changes in frequency, as noted above. Further physical examination reveals no abnormalities. The urine is quite negative.

Clinical Diagnosis. Mitral regurgitation; epilepsy.

This condition lasted until about the first of February, 1902, when the patient began to be troubled with increased shortness of breath and with palpitation of the heart on slight exertion. On account of these symptoms she was put to bed. The incompensation advanced, but very slowly, so that up to within three days of her death she did not consider herself very sick, and went about the ward without serious inconvenience. She was unable to take digitalis. Digitalin was tried, but without any appreciable effect. April 24th she had a sharp attack of diarrhœa, and on the morning of the 25th complained of severe, aching pain in the abdomen. At this time the abdomen was distended and loudly tympanitic, except low in the flanks, where there was dulness. During the morning she had a severe epileptic seizure, and later two minor attacks. Following these she was somnolent for nearly twenty-four hours, with extremely feeble and irregular pulse and great prostration. On the 26th she was brighter. The pulse, however, was scarcely palpable, and it was noticed that there was œdema of the eyelids and of the ankles. This œdema increased during the day, and the patient died, with increasing weakness, at 6.15 A.M., April 27th. On consulting the list of her attacks it is noted that in November, December, and January she had one seizure per month, two in February, and one in March. In April there was one on the 17th, and the three already spoken of on the 24th.

Epitome of Post-mortem Findings. L. H., died 6.15 A.M., April 27, 1902. Autopsy (by the writer) begun 1.30 P.M. same day. There is a slight icterus of the skin and mucous membrane. The fingers and ears are livid, and the rigor is beginning in the fingers. There is moderate œdema of the face, especially of the eyelids, and slight swelling of the ankles. A small quantity of rather deep yellow, clear fluid escapes from the abdominal cavity. The liver extends one-third of the way to the umbilicus and as far to the left as the spleen, to which it is attached over a small area by rather tough adhesions. The parenchyma of the organ is grayish in color, mottled with small, red islands; it weighs 1210 grammes (40 ounces).

The spleen weighs 250 grammes (8.3 ounces), and is very firm. The kidneys are about the normal size. The capsule strips off rather easily, leaving a somewhat roughened surface. On section, the cortex is pale, the pyramids stand out prominently, and their radiating vessels are plainly visible as dark lines.

Both lungs are bound to the chest wall by many rather tough adhesions. There is a moderate quantity of fluid in each pleural cavity, more in the left. The lower lobe of the left lung is compressed and heavy, and contains one small patch of consolidation. The upper lobe of this lung and the right lung are quite œdematous. The weights are: Right lung, 575 grammes (19 ounces); left lung, 400 grammes (13 ounces).

The pericardium is free from the heart except for a small area over the upper posterior surfaces of the auricles, where it adheres slightly; the rest of its surface is smooth. There are 70 c.c. (2 ounces) of yellow-

ish, slightly turbid fluid in the pericardial sac. There are a few petechiæ over the posterior portion of the auricles. The heart, which is very soft, weighs, when freed of the soft, dark clots that filled the auricles, 515 grammes (17 ounces). All the chambers are dilated. The fresh organ measures 15 x 11½ cm. (6 x 4.5 inches). When the heart, which was hardened whole, was subsequently cut, all the valves were normal except the mitral. The anterior flap is somewhat thickened, but not shortened. The posterior one is thick and very short, and in its middle portion represented by a low, hard ridge, which bears a few small, hard, old vegetations. The left ventricular wall at its thickest portion measures 1.3 cm. (½ inch), and interventricular septum 1.7 cm. (6 inches).

There is no hemorrhage from the scalp incision. The skull is rather thick. The brain weighs 1130 grammes (37.6 ounces), and is to all appearances normal; there is no increase of fluid in the meninges. The cerebral arteries are collapsed and soft.

Anatomical Diagnosis. Chronic mitral endocarditis, with insufficiency. Hypertrophy and dilatation of heart. Chronic passive hyperæmia of liver, spleen, and kidneys.

In this instance the sequence of events is certainly very suggestive. The patient's history of chorea and afterward rheumatism and the heart trouble beginning simultaneously with the attacks, might easily give color to the theory that there was a heart lesion due to the early infectious diseases, and that when it reached a certain stage it provoked the epileptic seizures. The fact that a sister, also a victim of early chorea, died in a fit, adds to the interest.

It will be seen that there was but little difference in the frequency of the attacks during the months that the patient was in her usual health—November, December, and January, for example—as compared with the three months when the compensation was not good—February, March, and April. It seems not unreasonable to suppose that the seizures occurring on the 25th of April had as a direct result an acute dilatation of the heart, which was the immediate cause of the patient's death.

Case V.—L. W., female, aged thirty-two years, English; admitted January 24, 1900. So far as known, there is no family history of nervous disease. When she was fourteen years old she was ill with what seems to have been an attack of acute rheumatism. She was in a hospital for some weeks on account of swollen and extremely painful joints. Her epilepsy began at twenty-one years. At first the attacks were only nocturnal; now they occur both day and night. About the same time the patient began to have trouble with her heart, and since then has been rather short of breath and has had more or less pain. Once she was sick in bed nearly two months, she says, on account of shortness of breath. While in the hospital she has had hysterical attacks, beginning with an acceleration of respiration, followed by fixing of the eyes and moderate opisthotonic spasm and convulsive movement of the arms. There are also frequent attacks that resemble in appearance genuine grand mal; these occur mostly at night. There have also been several periods of mental disturbance, during which she is excited and has well-marked delusions. Lately she has been in bed for several months on account of shortness of breath. There are frequent attacks of vomiting, so that she is nourished with great difficulty. Her general nutrition, however, remains good, and there is little change from

month to month. This patient has been given digitalis on several occasions, but it was always necessary to discontinue it promptly on account of the condition of the stomach. At no time could it be noted that the condition of the heart had the slightest effect on the frequency or severity of the seizures.

The patient is rather under the medium size, with a slender but symmetrical thorax. The skin is pale, but the finger-nails are slightly cyanotic. There is no œdema. Examination of the lungs shows râles of various sorts, but no dulness. The breath sounds are vesicular; the respiration is about 40, and there is frequent, loose cough. The abdomen is flat, tympanitic, and neither the liver nor the spleen are palpable. There is a faint pulsation in the epigastrium, but none in the neck. The apex-beat is in the fifth intercostal space, about in the mid-clavicular line. It is plainly felt, but not thrusting. The second sound in the pulmonary area is easily felt as a sharp click. There is a coarse presystolic thrill in the apex region. The rhythm is frequent (130) and there is occasional asystole. The absolute dulness begins above, on the fourth rib, and is enlarged to the left about a finger's breadth. To the right it extends just under the sternal border. At the apex there is a loud, coarse, presystolic murmur, ending abruptly in the very much exaggerated first sound. This murmur is not heard inside the nipple line, but is rather well transmitted into the axilla. There is also a systolic murmur less loud than the diastolic. This bruit is not so well heard in the axilla, but increases toward the right, and is loudest at the base of the ensiform cartilage. It is also easily followed upward to the second right interspace. In the area of the pulmonary valve there is a systolic murmur, but of coarser quality and very loud second sound. In the first intercostal space on the right, and in the carotids, a blowing, systolic murmur is heard. The pulse is frequent, small, soft, and rather irregular. The urine shows a trace of albumin and rather numerous casts, clear, and with granules.

Clinical Diagnosis. Double mitral lesion; disturbed compensation; epilepsy; hysteria; mania.

The next two instances concern rather older patients, but the absence of any arterio-sclerosis seems to place them rather with the juvenile than with the senile cases. One of them certainly, and the other probably, belongs to the class of late epilepsies (Mendel)—that is, epilepsy of onset after forty years. In the first the history of the epilepsy was very unsatisfactory; but the tonic spasms, together with the anatomical findings, make it possible that the patient had epileptiform seizures of cardiac origin. The absence of autopsy in Case VII. made it impossible to confirm the diagnosis of chronic myocarditis or to exclude changes in the brain. The history, however, is strikingly suggestive. This case furnishes a good example of the absence of seizures during the period of failing heart.

Case VI. was reported by Ohlmacher[43] as an illustration of one of the consequences of myocardial degeneration following coronary artery sclerosis. It was regarded as an example of so-called "cardiac

epilepsy," and seems to bear so directly upon the matter here in hand that I have given, in a somewhat abridged form, Dr. Ohlmacher's report.

S. C., male, laborer, colored, aged fifty-five years. No family history could be obtained aside from the fact that the patient's mother died suddenly at an advanced age. The patient himself has had rheumatism, pneumonia, and soft chancre. For some time he has had epileptiform attacks, in which he would fall suddenly, become unconscious, and remain in a state of tonic spasm for some minutes. Such fits were frequent. February 14, 1898, he was admitted to the Cleveland General Hospital, with an attack of pneumonia. The night before he had a severe chill and fell to the floor, where he was left for some minutes, it being supposed that he was in one of his fits. Physical examination reveals the signs of right-sided pneumonia. The apex-beat is in the sixth intercostal space, two fingers' breadth outside the nipple line. The heart's dulness is enlarged both to the left and to the right. A systolic murmur is heard in all the cardiac areas, but loudest at the apex. The diastolic sound is clear. There is a pericardial friction rub in the fifth intercostal space, in the left nipple line. Death took place February 21st, before the crisis. The exact nature of the heart lesion was not appreciated during life.

The autopsy was performed fourteen hours after death. The principal changes aside from those of the heart are referable to a croupous pneumonia in the stage of red hepatization, involving the lower and middle lobes of the right lung.

The apex of the heart is displaced decidedly to the left. In the pericardial sac a small amount of straw-colored fluid with yellowish flocculi is found, and the thickened heart's covering is intimately coherent about the much elongated apex, serving to strengthen and protect this portion, which proves to be a chronic cardiac aneurism. The organ weighed 745 grammes (24.8 ounces) when freshly removed. From base to apical extremity the organ measured 17 cm. (6.6 inches) as compared with 9 to 10 cm. (3.9 inches), the average length of the normal adult human heart. On examination it is found that this increased extension is mostly due to a prolongation of the left ventricle, in the form of an ovoidal sac about 7 cm. (2.7 inches) long and 6 cm. (2.4 inches) wide. There is also considerable hypertrophy of the left ventricle, whose wall measures 2.5 cm. (0.9 inch) in thickness. On incising the heart the nature of the ovoidal prolongation becomes more apparent, and it is now seen to be a sac with a dense fibrous wall, in which traces of heart muscle still remain, about 3 mm. (0.1 inch) in thickness, filled with a firm, partly calcified thrombus. Section of this thrombus, whose protective function in compensating for the aneurismal dilatation of the ventricle is evident, shows a pretty red and white lamination, the uncolored portion being the most calcified. On the removal of the thrombus the aneurismal pouch is found to be in full communication with the left ventricle. Induration of the myocardium is pronounced in the ventricular wall adjoining the aneurism, and patches of fibrous myocarditis are scattered pretty generally throughout this left ventricle, being especially marked in the papillary muscles. The aorta exhibits a condition of advanced atheroma, and the left coronary artery is likewise affected, being tortuous, stiff, and nodular, with calcareous patches within. At the point

where this vessel divides into its two main branches the sclerosis has advanced to the point of completely obliterating the lumen.

As the cranium was not opened, the important question of lesion of the cerebral substance, or disease of the cerebral arteries, cannot be decided.

Anatomical Diagnosis. Sclerosis and obliteration of left coronary artery, with fibrous myocarditis and aneurism of heart; pneumonia.

Case VII.—C. C., carpenter; admitted to the Ohio Hospital for Epileptics, October 28, 1898. So far as known, there is no history of neurotic affection in the family. The patient underwent an attack of inflammatory rheumatism at twenty-eight years. From that date until he was forty-five years of age he was, as a rule, well and strong, his only other illness in the interval being an attack of ague. During this year he had his first epileptic attack after an unusually hard day's work. This seizure began with a cry, and when he was seen by his wife, a few minutes later, he was quite black in the face. This fit was at the time attributed to some difficulty with the heart. After this the attacks continued at irregular intervals during the rest of his life. As a rule, they began with a cry, and the patient would fall in a convulsion, frequently biting the tongue, sometimes frothing at the mouth. During his hospital residence he had at first three or four seizures a month, to all appearances those of ordinary idiopathic epilepsy. The attacks grew less frequent, and in the last few months were entirely absent. For some time after admission the patient was in moderately good health, but complained of fatigue on exertion. About October 1, 1900, signs of incompensation began to manifest themselves, and October 15th he took to bed with the fatal illness. At this time there were present signs of failing heart, as follows: œdema of legs, icteric-cyanotic skin, and dyspnœa. The apex-beat could not be seen, but a fluttering impulse was felt two fingers' breadth outside the nipple line; the rhythm was extremely irregular and very frequent. The dulness began on the fourth rib above, extended to the nipple line and to the right edge of the sternum. All the heart sounds were audible and flapping; the first sound at the apex was accompanied by a loud, sawing murmur, which was quite sharply localized to this area (at an examination of the heart, several weeks before, no murmur could be heard, and the heart seemed, as far as local signs went, normal). There was tenderness in the region of the liver, but neither this organ nor the spleen could be felt.

From this time the patient slowly sank. Later there was effusion into the pleural cavities, and he died December 27, 1900. No autopsy.

Clinical Diagnosis. Chronic myocarditis, with incompensation; epilepsy.

Of the late epilepsies, most of our cases had besides heart lesions marked arterio-sclerosis, as a rule involving the cerebral arteries. The three instances next following seem to offer the ideal condition laid down by Schupfer.*

* Our plan for a detailed study of these brains was defeated by the fire that destroyed the laboratory, with all the preserved specimens, leaving available only the immediate autopsy notes.

CASE VIII.—F. M. T., farmer, aged sixty-five years, entered the hospital January 3, 1896. His father is said to have been an epileptic. The patient has always worked hard. No other fact of importance in the history. The attacks began at the age of sixty-two years, and occurred thereafter at intervals of three or four months. They resembled ordinary grand mal, preceded, as a rule, by a cerebral aura. The patient's heart was frequently examined during his stay at the hospital, and showed well-marked signs of mitral regurgitation. He was considerably demented, and this condition increased rather rapidly in the last six months of his life. October 30, 1899, the patient slipped and fell upon the floor, fracturing the left hip. About a week later a left-sided hemiparesis appeared, with partial unconsciousness and slight elevation of temperature. During the next two days the stupor slowly deepened, the paralysis became more marked, while the temperature sank to subnormal. Death occurred December 8, 1899.

Clinical Diagnosis. Mitral insufficiency; fracture of hip; apoplexy; epilepsy.

Autopsy. Begun December 8, 1899, one hour and fifteen minutes after death. The mucous membranes are pale, the skin is sallow, and there is œdema of the feet and legs. There is no rigor mortis. The left leg is shorter than the right and everted, due to an old injury of the ankle and a recent ununited fracture of the neck of the femur. On opening the skull it is noted that the incision through the frontal bone bleeds freely. The subdural fluid is increased in amount, and the pia is œdematous. The arteries of the cerebrum are all atheromatous. Both middle cerebrals contain soft, red clots, that in the left side being more compact than in the other. The brain weighs 1300 grammes (43.3 ounces). There are small foci of red softening in the knee of the left internal capsule, and a more recent one, about the size of a split pea, in the right thalamus, in the area of the anterior tubercle. The whole left corpus striatum is less rotund and somewhat softer than the opposite corresponding area. There is no increase of fluid in either the thoracic or abdominal cavities. The lungs together weigh 790 grammes (26.3 ounces); the left one adheres. Both, particularly the left, are tough, dry, red, and emphysematous, with patches of atelectasis. The heart, which weighs 570 grammes (19 ounces), is hypertrophied, especially as to the left ventricle. The muscle is paler in color than normal, and rather soft. There are scars of fibrous myocarditis in the wall of the left ventricle, most marked in the papillary muscles. The posterior flap of the mitral valve is held down by the thick, pale, stiff muscle and its short chorda. The segments of the valve are thickened and white, but not shortened. The same is true of the aortic valves. There are opaque spots in the endocardium of the left ventricle, and in the walls of the coronary arteries are raised, yellowish, firm plaques. The aorta measures 12 cm. (4.7 inches) at the orifice, and continues as a localized aneurismal widening of about this size to the arch. The wall is inelastic and quite thick, and the intima is pale, with soft, yellowish sclerotic patches. The liver weighs 1940 grammes (64.6 ounces), is hard, but the substance is friable. The lobules are prominent. The capsule is thick and sticks. Both the kidneys weigh 340 grammes (11.3 ounces). They are somewhat nodular, and both contain several arterio-sclerotic cysts. The parenchyma is mottled red and yellow. The cortex is about a third narrower than

normal. The vessels are prominent, especially the straight ones. The capsules adhere.

Anatomical Diagnosis. General arterio-sclerosis; sclerosis of the cerebral arteries; hemorrhagic softening of the knee of the left internal capsule; recent red focal softening of the right optic thalamus; coronary sclerosis; fibrous myocarditis; insufficiency of the mitral valve, with hypertrophy of the left ventricle; cylindrical dilatation of the aorta; arterio-sclerotic atrophy of the kidney; chronic hyperæmia of the spleen; cyanotic induration of the liver; emphysema, atelectasis, and passive hyperæmia of the lungs.

Case IX.—This and the following instance were reported *in extenso* by Ohlmacher[44] in his studies on the pathology of epilepsy. While the possible relation of the circulatory affection and the epilepsy was spoken of, the striking disease of the vascular apparatus makes them appropriate for consideration in this connection.

I. S., aged fifty-seven years, single, was admitted to the hospital March 26, 1897. The patient came from a soldiers' home, and the history of epilepsy was very unsatisfactory. Nothing can be ascertained as to the family history. It was claimed that he had suffered with epileptic convulsions for seven years before his admission here. He presented all the symptoms of chronic heart disease, eventuating in the phenomena attending broken compensation. He had two attacks shortly after entering the hospital, but none in the last three months of his life.

The autopsy was made five hours after death. A pronounced œdema existed in the trunk and limbs, especially marked in the scrotum, which was enormously swollen. The face is moderately œdematous and livid, and the mucous membranes are deeply injected. A great deal of dark fluid blood escapes from the various incisions, especially about the head. There is an extensive dropsy of all the serous cavities. The right lung weighs 520 grammes (17.3 ounces); the left, 429 grammes (14.3 ounces).

Heart. Weighs 725 grammes (24.1 ounces). Both pericardial layers are roughened in spots, especially about the base of the heart. The organ lies transversely, the apex being 4 cm. (1.5 inch) outside of the left nipple line in the sixth costal space, while the base extends somewhat below the sternal border. The right auricle and ventricle are dilated and distended with fluid blood and soft, red clots; the left side is more nearly empty. The endocardium is opaque and thickened, especially in the left side, about the valvular rings. The myocardium is very firm, lighter in color than normal, and on close inspection shows white, glistening fibrous areas dispersed in the muscular walls, and particularly noticeable in the muscular papillæ of the left ventricle, where a variegated appearance is given to the cut muscular surface.

The aortic valves are competent to the hydrostatic test, and the orifice is normal in circumference (7.5 cm.) (2.9 inches). Above the valve the vessel gradually dilates until it becomes a tube measuring 11 cm. (4.3 inches) in circumference. This dilatation continues over the arch to the descending aorta, where it gradually recedes. Upon the interior of the aorta a general roughness is produced by the yellowish or whitish, firm and often calcareous plaques which are here disposed. In some places these elevated patches have been worn away to leave ragged, punched-

out areas. This atheromatous condition is not so well pronounced in the aortic tributaries as is usually the case where this vessel is so profoundly affected. A marked stenosis of the orifices of the aortic branches, especially the coronaries and the innominate exists, and in the case of the right and left coronary arteries this stenosis has advanced until the aortic orifice of these vessels is only large enough to admit the body of an ordinary sized pin. Immediately beyond the strictured opening the coronary vessels dilate considerably. The lining of these arteries is almost free from sclerotic change, and no localized thickening or attempt at occlusion by thrombosis can be found in them. It appears that the fibrous degeneration resulted from this stenosis of the coronary orifices instead of, as is usually the condition, from a sclerosis or thrombosis of the vascular channels proper. The other visceral changes were cyanotic induration and arterio-sclerotic atrophy of the liver, spleen, and kidneys.

Brain. The whole fresh organ weighs 1380 grammes (46 ounces). Beyond a moderate dropsical condition of the meningeal spaces and of the ventricles and a general anæmia of the brain substance, no gross changes are apparent. A very slight degree only of sclerosis is visible in the basilar arteries, though they are dilated more than is ordinarily the case. Cultures were negative.

Anatomical Diagnosis. General arterio-sclerosis; atheroma and cylindrical aneurism of the aorta; stenosis of the coronary orifices; interstitial (fibrous) myocarditis; hypertrophy and dilatation of the heart; brown induration of the lungs; general œdema and hydrops; arterio-sclerotic atrophy and passive hyperæmia of the kidneys, spleen, and liver.

Case X.—E. H., white, married, aged sixty-seven years; admitted October 1, 1894, from a county infirmary. He died May 8, 1898.

The patient is in good nutrition, and his general health is fair. No family history can be obtained. His epilepsy began in the fifty-fifth year of life, "while working hard in warm weather." The paroxysms have been irregular in occurrence since that time, usually separated by intervals of two or three months, and then coming in groups of two or three. The patient claims he was addicted to the use of morphine for some twenty years, but gave it up a few years ago, after which the epileptic attacks were not so frequent.

Since admission most of the attacks have occurred at night, and are described as grand mal in type, though only the attendants' and patient's statements are in evidence on this point.

Sunday morning, May 8th, he got up at 5 o'clock and began dressing, remarking to one of the other patients that he had a "spell" in the night, and that he did not feel well. At the attendant's suggestion he returned to bed, and an hour later was found gasping for breath and moribund, expiring almost immediately. A patient who was nearby said H. was sitting on the edge of his bed, when he suddenly fell backward, without a moan, and began gasping.

The autopsy showed marked alterations in the cardiovascular system and in the brain; the other organs exhibited only the ordinary changes of arterio-sclerosis.

Heart. Weighs 320 grammes (10.6 ounces). The right cardiac cavity contains a moderate amount of fluid blood and post-mortem clots, while the left side is contracted and almost empty.

The aortic orifice measures 9 cm. (3.5 inches); mitral, 8 cm. (3.1 inches); tricuspid, 10 cm. (3.9 inches); pulmonary, 7 cm. (2.7 inches). Several opaque and thickened spots appear in the epicardial surface of the left ventricle. The endocardium of the right side is not altered, but that of the mitral and aortic rings is thicker and more opaque than normal, though these valves seem to retain their competency. Both coronary arteries are the seat of extensive sclerotic deposits, which here and there tend to narrow the calibre of these vessels, not, however, producing complete obliteration of the lumen in any one point, and there is no thrombotic plugging. The myocardium, especially of the left ventricle, is tough and pale, and on section shows white, fibrous bands and scars in the muscular substance, these streaks being especially prominent in the papillary muscles.

Arteries. The aortic wall is everywhere thickened and inelastic, while its lining is the seat of extensive whitish or yellowish, firm, sclerotic deposits, many of which are calcareous and rough. Just before its division into the iliacs the aorta is converted into a rigid calcareous tube. At the junction of the ascending portion and the arch a hemispherical aneurismal sac bulges from the front (ventral) and right side of the aorta, being about the size of a walnut, and communicating with the artery by a narrowed neck. The walls of this sac are firm, and it is filled with a partially organized and roughened thrombus. A constricted or stenosed condition marks the orifices of most of the aortic branches, being especially evident in the left subclavian, whose orifice is reduced to a mere slit. As the right internal carotid comes through the carotid canal it is entirely calcareous, and is plugged with an organized clot extending to the point at which this vessel divides into its cerebral branches. Much the same appearance is presented by the vertebrals, and that on the right side is occluded by a firm clot, which extends into the basilar artery. Both the vertebrals, the basilar, and several of the smaller cerebral arteries are here and there dilated into small aneurisms, and all these vessels are more or less sclerotic.

Brain. The entire fresh encephalon weighs 1350 grammes (45 ounces). The venous sinuses are filled with dark blood, while the arteries of the pia-arachnoid contain an unusually small amount of blood. The dura is thicker and more opaque than usual, clings closely to the skull, and adheres so tightly to the pia-arachnoid as to make its separation difficult, this being particularly marked about the frontal lobes. The soft meninges are generally opaque and thickened in patches, and cling to the cerebral substance with unusual persistence. Over the inferior aspect of both frontal lobes a series of vesicles filled with clear fluid is seen in the arachnoid, and beneath them the frontal gyri are much shrunken and hardened. As a whole, the cerebral substance feels harder than usual, and at the junction of the parietal and occipital lobes on the right side several of the gyri are shrunken, like those just described for the frontal lobes. No alteration is found in the ependymal cavities, and the basal ganglia are intact.

The bacteriological examination was entirely negative.

Anatomical Diagnosis. General arterio-sclerosis; saccular aortic aneurism; fibrous myocarditis; pulmonary emphysema and œdema; sclerosis of cerebral arteries; sclerosis of frontal lobes of cerebrum; miliary cerebral aneurism; embolism of right internal carotid and vertebral arteries.

Similar to the last case, but with very slight brain lesion, probably not more than could be accounted for by the atrophy due to the patient's advanced age, is Case XI. Indeed, it is doubtful if this patient could not properly be put among the simple heart epileptics.

Case XI.—M. K., aged seventy-eight years, formerly a domestic, for two years a resident at the hospital, died December 12, 1900, after a long period of failing compensation. No family history of neurotic affection could be elicited. The patient's own mental condition was good. The first epileptic seizure occurred in the sixty-third year. There were but few severe attacks while the patient was under observation, and they seemed in all respects like ordinary grand mal. The victim would fall in a convulsion, frothing at the mouth, become quite cyanotic, and afterward usually sleep for an hour. There were also frequent atypical attacks which began with irregular movements of all the muscles of the body. She would pick at her clothing, the face would twitch and become quite cyanotic. She was evidently unconscious for a few seconds, and sometimes fell. These minor seizures were accompanied by twitching movements of the hands and face. During the year just prior to the patient's death she had on an average seven or eight attacks per month. In the last four months of her life, however, the average sank to between four and five. Aside from the fact that the patient had a valvular lesion and hard arteries, the nature of the heart affection was not appreciated during life. The urine was quite negative.

The autopsy, performed October 23, 1900, resulted as follows: The body is that of a fat woman, 160 cm. (63 inches) long. The lips and ears livid and the mucosæ injected. The skin of the trunk, arms, and legs are pits on pressure, and is pale and waxy looking. There is a very thick layer of pale fat, and the muscles are also pale. The brain weighs 1230 grammes (41 ounces). The dura sticks to the skull-cap with great tenacity. This membrane is rather thin in front and behind, but is thick at the sides and in the tentorium. There is an increased amount of clear fluid beneath the dura and pia. The pia is opaque in patches. The cerebral convolutions are small and flattened. The cerebellum is relatively small and its convolutions irregular. The heart adheres over its whole surface to the pericardium, obliterating the sac, but it is easily torn free. The organ weighs 485 grammes (16.1 ounces). The auricles, especially the left, are dilated, and the heart muscle is flabby. The mitral orifice is stenotic, admitting but one small finger-tip. One of the aortic cusps is thick and firm, and there is moderate dilatation of the aorta. Both ventricles, especially the left, are dilated and hypertrophied. There is one small adhesion over the right lung posteriorly; the left pleural sac contains about eight ounces and the right about a quart of clear, serous fluid. There is marked general venous stasis. The lungs together weigh 850 grammes (28.3 ounces), are dry on section, dense and reddish from the marked stasis in the pulmonary veins, of which the largest one contains a red clot. The liver weighs 1300 grammes (43.3 ounces), is dark in color, with whitish islands under the capsule. The organ is soft, and on section there is general pallor, and the lobules stand out distinctly, with great engorgement of the central veins. The gall-bladder is converted into a solid, pyriform mass, almost stony in its hardness.

The pancreas is closely invested with fat, and contains numerous yellowish or white foci as large as a pin's head, especially in the region of the head of the organ. The kidneys together weigh 240 grammes (8 ounces); the capsule sticks slightly, while the cortex looks rather narrow. No other abnormality can be seen. The intestines are deeply congested, giving the mucosa a deep purplish, almost black, hue.

Anatomical Diagnosis. Adherent pericardium; mitral stenosis; aortic insufficiency; hypertrophy and dilatation of the heart; general venous stasis; hydrothorax; œdema; passive venous hyperæmia of the spleen, kidneys, brain, stomach, and intestines; cyanotic induration of the lung; cyanotic atrophy and fatty infiltration of the liver; ancient cholecystitis, with obliteration of the gall-bladder; disseminated peri-pancreatic fat necrosis.

Conclusions. We have been unable in any of our cases to show to our own satisfaction that there was any direct connection between the vascular lesions and the epilepsy. The sequence in several of the heart (juvenile) cases that we have selected is suggestive. There was, as a rule, a clear history of acute infectious disease—rheumatism in Cases I., III., V., VI., and VII.; rheumatism and chorea in Case IV. These infections were followed by heart lesions, several times with symptoms on the part of the heart before the onset of the attacks, and, finally, by epileptic seizures. It must not be forgotten that these cases were chosen from a larger number, precisely for the reason that the order in which the symptoms appeared seemed to lend color to the theory that they might be causally related. The fact that several of the patients had atypical seizures has some interest, in view of the fact that similar seizures can be brought on by artificially induced anæmia of the lower brain centres. Only one of our cases had cardiac aura (Case IV.), and these are so common among epileptics as to deprive this fact of much significance. In those cases where there seemed to be an indication on the part of the heart for the administration of digitalis we were unable to see that its use had any appreciable effect upon the attacks. It must be said, however, that in none of these instances was there any noteworthy improvement in the condition of the heart. At no time did the increasing severity of the heart disease seem to occasion a corresponding increase in the frequency of the attacks. On the contrary, it several times (Cases VII., VIII., X.) seemed quite clear that as the heart condition grew progressively worse the attacks grew less and less common or were absent altogether, following the general rule in the case of intercurrent affections in epilepsy. Too little is known of the real condition of the cerebral circulation during the attacks, and the results of experimentation have been too confusing to allow us to say from empiric grounds that any circulatory condition likely to result from heart disease could be the cause of the attacks; so that, so far as the pure cardiac cases are concerned, it seems to us more than doubtful if the occurrence of heart lesions in epilepsy is

anything more than a coincidence. At least the verdict of "not proven" must stand for the present.

In the senile cases with sclerosis of the encephalic arteries the evidence, at least from the literature of the subject, is stronger. In our own experience we have found so far no good reason, aside from the fact that the heart lesion antedated the onset of the fits, for thinking that the latter were the result of the cardiac affection. If this were true it would be surprising that a much larger number of old people do not have epilepsy. Even if the two things are correlated, we should be inclined to lay the greater stress upon the changes in the cerebral vessels, so that even here the part taken by a diseased heart, if a factor at all, is an ancillary one.

In fine, we do not discover that there is any satisfactory direct proof that cardiovascular disease is a cause of epilepsy; therefore, the demonstration of their connection must rest upon methods of exclusion. This being so, we can hardly do better in the present state of our knowledge than adhere to the postulates of Stintzing:

1. The heart disease must precede the epilepsy.
2. Other causes must be excluded.
3. The coincidence must be frequent.
4. Improvement in the heart disease must improve the epilepsy.

These conditions seem to be reasonable ones, and could be fairly used as a test of the causal relationship of any one disease to another. Let us inquire how far they are met in the present instance.

That the causative disease must precede the other goes without saying, and this first condition is satisfied in many cases. That the fourth condition is also met is witnessed by a large number of recorded cases, although our own series has been too limited to furnish an example.

Although some observers find a large proportion of heart lesions among epileptics, most of the authority and our own experience point strongly to the fact that the coincidence of the two diseases is not very frequent. While this condition may be objected to as not essential to the proof, its non-fulfilment seems to us strong negative evidence.

The second postulate imposes the most difficult condition, as it does not seem possible, in the present state of our knowledge concerning the etiology of epilepsy, to exclude all other causes. Upon the whole, then, we must consider these postulates as not fulfilled; and while some authors think they can demonstrate that heart disease is a cause of epilepsy, it seems to us that this is by no means proved, and that a study of the recorded cases and of our own examples does not tend to establish the proposition that cardiac disease and grand mal stand in a causal relationship.

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HYDATIFORM MOLE: WITH A REPORT OF TWO CASES AND CLINICAL DEDUCTIONS FROM TWO HUNDRED AND TEN REPORTED CASES.*

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Synonyms. Hydatiform degeneration of the chorion; uterine hydatids; vesicular mole; myxoma chorii; blasenmole; cystic mole; hydatid mole; dropsy of the villi.

The History of Hydatiform Mole. In a valued contribution by R. Kossman, Berlin, we are given in the German text translations of the original manuscripts on hydatiform mole from the time of Ætius von Ameda,[1] in the early part of the sixth century, to the time of Virchow, in the latter part of the nineteenth century. This literal translation of the writings of Ætius will be of historical interest.

"*Concerning the Hydropic Uterus.*

"When the monthly bleedings have been absent for a considerable time, and impregnation thereby prevented, then it follows that an outpouring of fluid occurs into the uterine cavity. At times certain bodies appear in the uterus, which resembles a gall-bladder somewhat, and in which the accumulated fluid is contained.

"There ensues, therefore, on the part of the sufferer an extensive spongy swelling, somewhat resembling a gaseous inflation in the lower abdominal region; and also a rumbling, such as occurs in the bowels; a feeling of weight when walking; labored respiration; foul-smelling stools; absence of monthly bleedings, and conception and irregular flowing. If the separation is especially violent, the small bodies which resemble cysts at times rupture, and from them escapes a water-colored, tough fluid.

"For the patient in whose uterine cavity the fluid is retained—and this is clearly shown by the symptoms—one must order rest in bed, emetics, and powerful enemata."

In the above text it is probable that Ætius referred not only to hydatiform mole, but also to hydramnios and missed labor.

The next account of hydatiform mole is given by Christoph á Vega,[2] who advanced the theory that the sacs filled with fluid were the product of the union of the maternal humor with the male semen in the uterus. From the time of Christoph á Vega references to hydatiform mole are found with increasing frequency—many of them curious and amusing.

* Read before the Chicago Gynecological Society, November 21, 1902.

Hippocrates was evidently acquainted with the condition as a cause for abortion. He states that when the "cotyledons" fill with mucus the menses become scanty; and if the woman becomes pregnant, abortion occurs after the embryo has attained considerable size.

In 1690 Antonius Vallisnieri[3] wrote in a letter to Malpighi a description of a miscarriage complicated by hydatiform mole. He expressed his doubts as to the origin of the mole, but the vesicles escaped unnoticed along with the blood, or else arose from the placenta itself. Later Malpighi expressed the view that the cysts replaced the chorion. Valleriola applied liniments and potions, and finally tied a "lapis ætitus" to the left leg. This "at once produced expulsion of the mole." He believed the mole to have originated from the female seed, or ovum, which was not impregnated during coitus because of the escape or destruction of the male germ.

Percy[4] regarded the vesicles as animals (tænia hydatidena of Pallas), and says he has seen them move when exposed to the action of vinegar and salt. Madame Boivin[5] believed them to be the degenerated product of unimpregnated ova. Goeze,[6] in 1782, suggested the parasitic nature of the lesion. Ruysch thought a retained placenta was essential to the formation of hydatiform mole. Dewees[7] speaks of the vesicles as animals of "extremely simple organization and function."

In 1795 Gregorini[8] reported a case of hydatiform mole in which metastatic growths appeared in the lungs. This is probably the first recorded case of syncytioma malignum arising from hydatiform mole. The thesis is illustrated by a sketch of the mole, together with a fœtus.

It is interesting to note that as late as the early part of the nineteenth century it was believed[6] that conception was not essential to the development of a hydatiform mole. Dating from the writing of Velpeau,[10] the lesion has been universally recognized as a degeneration of the chorionic villi. Since then it has been a question as to the cause of the degeneration of the chorionic villi and the character of the degeneration. Virchow[11] may be credited with having advanced the modern theory as to the pathological nature of hydatiform mole, though his views are not universally accepted. (See later.)

Etiology. Nothing definite is known of the immediate and remote causes of hydatiform mole. The age at which it commonly occurs is said to be near the end of the childbearing period. According to Bowin, 25 per cent. are found between the ages of forty and forty-six years. Schroeder reported one occurring at seventeen years of age. From the accompanying tables it is seen that the average age is twenty-seven years; that the extreme ages are thirteen and fifty-eight years, and that the greatest number occur between the ages of twenty and thirty years. As to the frequency of recurrence, it is not unusual for a woman to give birth to a second mole some months or years after the

expulsion of the first. In the second case here reported there was an interval of about twenty months between the expulsion of the first and second mole. Fritsch records a case in which there were four moles successively developed. Majer records eleven moles and a single child born of one woman.

It is stated that syphilis, anæmia, heart and kidney lesions, and tuberculosis are general predisposing factors in the production of hydatiform mole, but proof of this is wanting. The question as to whether the lesion is of maternal or of fœtal origin is not fully settled. In favor of the view of the maternal origin may be mentioned the recurrence of the mole in the same individual and by different husbands; the common occurrence late in life; the partial vesicular degeneration of the chorion in the presence of a perfectly healthy fœtus; the common occurrence of cystic degeneration of the ovaries associated with hydatiform mole; and lastly, that endometritis and nephritis commonly precede the development of hydatiform mole. In favor of the fœtal origin is the fact that in twin pregnancy one mole alone may be involved in the cystic degeneration of the chorionic villi. If, as has been stated, death of the fœtus is a cause for vesicular degeneration of the chorion, how are we to account for the rarity of the lesion in cases of missed labor and abortion, where the fœtus has remained dead for weeks and months in the uterus? The fact that in partial vesicular degeneration of the villi the fœtus may remain perfectly healthy forces us to the more probable conclusion that extensive vesicular degeneration of the chorion results in the death of the fœtus. Contrary to the evidence advanced in support of the theory of maternal origin is the occurrence of many moles prior to the formation of the placenta, at a time when there is not an intimate anatomical relation of the mole to the uterine wall. Marchand holds that hydatiform mole occurring early in fœtal life can be ascribed to a primary change in the ovum. He does not deny the possibility of other causes operating to produce partial degeneration of the chorion, and admits as highly probable that malnutrition has much to do with the development of the mole.

Van der Hoeven[12] examined ten hydatiform moles, of which nine were in the third, fourth, and fifth months of fœtal development; the tenth was in the first month. The last showed no vesicular degeneration of the reflexal placenta. Van der Hoeven reasoned that the ovum was healthy when it reached the uterus, and that it is possible that the disease was primary in the uterine wall, though not probable. In support of the theory of uterine origin he found degenerative changes in the endometrium. Virchow was the first to suggest the possible causal relation of endometritis to hydatiform mole. From the great frequency of endometritis complicating pregnancy as compared to the relative infrequency of hydatiform mole it is not likely that any direct rela-

tionship between the two lesions can be established. It would be difficult to determine whether the changes in the endometrium are primary or secondary to the development of the mole. Again, the histological changes in the endometrium associated with hydatiform mole are by no means constant. It has been suggested by Baumgart,[13] Marchand,[14] Kaltenbach,[15] Krentzmann, Runge,[16] Fraenkel,[17] and others that the tendency to cystic degeneration of the ovum may be referred to cystic degeneration of the ovaries. Each of the above-named authors has reported a case of hydatiform mole complicated by cysts of the ovary, and in a single case there was also a cystic kidney. In my second case both ovaries were cystic, each about the size of a man's fist. By reference to the accompanying table it is seen that in only 8 of the 210 cases were cystic ovaries recognized. The number of abdominal incisions made in these cases is few—a fact which possibly accounts for the above statistics. On the other hand, cystic degeneration of the ovaries is so commonly observed as compared with hydatiform mole that it is not likely that they stand in the relation of cause and effect.

Matwejew and Sykow[30] reported in the Gynecological Society of Moscow a case of tubal pregnancy in which the placenta had undergone cystic degeneration, and the ovary was likewise cystic. The patient was aged thirty-two years; she had had four normal labors and three abortions. The right tube contained the ovum, which ruptured about the eighth week of pregnancy. Symptoms of internal hemorrhage followed the rupture of the tube. Abdominal section revealed a large collection of blood in the pelvis, a ruptured tube, within which there was a hydatiform mole. The author stated that the cystic ovaries were undoubtedly the cause of the cystic degeneration of the placenta.

The following two cases have occurred in the practice of the author:

Case I.—Mrs. H., aged twenty-five years; married three years; a nullipara. Previous health always good; no menstrual irregularities; genitalia apparently normal. Had missed two menstrual periods, when she began to lose small quantities of blood. The bleeding continued to increase in amount and frequency, flowing profusely at night and but little during the day. This continued for about ten weeks, the patient becoming quite anæmic. There were the usual signs of pregnancy, and the growth of the uterus was somewhat more rapid than in ordinary pregnancy. The last of January, 1898, pain increased, hemorrhage became more profuse, and the uterus increased rapidly in size; during the night it extended two fingers' breadth higher. An examination revealed a bunch of vesicles protruding from the cervix. It was determined to enucleate the mole. A hypodermic of morphine was given; this was followed by vomiting and the spontaneous discharge of the mole, leaving no remnants in the uterus. Three years later the patient gave birth to a well-formed baby, the placenta being normal. The patient now enjoys perfect health, and is again pregnant. The mole showed a complete vesicular degeneration of the chorion; there was no evidence of a fœtus. The ovaries are apparently normal.

No menstrual irregularity or leucorrhœa has followed the expulsion of the mole.

Case II.—Mrs. N., aged thirty-eight years; married fourteen years; number of children, five; no abortions. Labor and puerperium normal at all times. Began menstruating at sixteen years of age; no menstrual irregularities; duration of flow, five days; no dysmenorrhœa; no leucorrhœa. Since the birth of her last child she has had two hydatiform moles. The first terminated by means of the curette at the end of the fourth month of pregnancy. The date of the last menstruation was April, 1898, and the mole was removed August 24, 1898. For two months prior to the removal of the mole there was a serosanguineous discharge, and the patient became weak and anæmic. The second mole was removed June 25, 1900, the last menstruation having been March, 1900. Her first symptom was a rigor, followed by a slight rise of temperature and a serosanguineous discharge, which began about June 6th. The uterus enlarged more rapidly than in normal pregnancy. In the light of the previous experience with a hydatiform mole it was believed that a similar condition existed. The patient was removed to the German-American Hospital. On examination the uterus was found to be symmetrically enlarged, extending one-third the distance from the pubis to the umbilicus. It was of doughy, elastic consistency, and freely movable. The cervix was patulous to the index finger. On either side of the uterus was a movable, cystic swelling, the size of a man's fist, and connected to the horn of the uterus by a pedicle. The conditions being not unlike those of the previous mole, and the debilitated condition of the patient demanding interference, it was determined to explore the uterine cavity. Ether was administered. Upon dilating the cervix small, transparent vesicles escaped, and the diagnosis of hydatiform mole was confirmed. In the effort to enucleate the mole the hemorrhage was alarming—so much so that the procedure was abandoned, the cervix and vagina packed with gauze, and a hysterectomy resorted to. A supravaginal amputation of the uterus was done, and the uterus with the mole intact, together with the tubes and both cystic ovaries, were removed. An uninterrupted recovery followed. The uterus when removed was uniformly soft and regular in outline. It measured 20 cm. in length, 18 cm. in the greatest transverse diameter. The wall of the fundus measured 1 cm. in thickness. Both ovaries contained multiple small cysts, enlarging each to about the size of a man's fist. The tubes were normal, and there were no adhesions or other abnormalities in the pelvis. On opening the uterus the mole was found almost completely enveloped in a firm coagulum of blood. The entire chorion had undergone vesicular degeneration; the vesicles were transparent and ranged in size to that of a hazelnut. Separating the mole from the uterine wall was a thin, tough, greenish-colored membrane. The placental site was located on the left anterolateral aspect of the uterus.

Microscopic Examination. *The Decidua Vera.* The glands do not differ essentially from those of normal pregnancy. In size, number, and general outline there is nothing unusual. The secreting epithelium of the glands is partially lost; the remaining cells are cubical or flattened. In the gland lumen are many desquamated and degenerated

epithelial cells and not rarely free blood and leucocytes. The decidual cells present no anomalies in structure; as in normal pregnancy they present a variety of forms, the greater number being polygonal or spindle-shaped. In the compacta they are more uniformly spindle-shaped, with elongated nuclei. Free blood together with groups of leucocytes are found between the decidual cells and in the musculature.

The Decidua Serotina. On the surface of the decidua serotina is a thin, fibrinous layer in which decidual cells are scattered. The decidual cells are round, polygonal, and spindle form, with large, round, granular nuclei. The glands are large, irregular in form, and the secreting

FIG. 1.

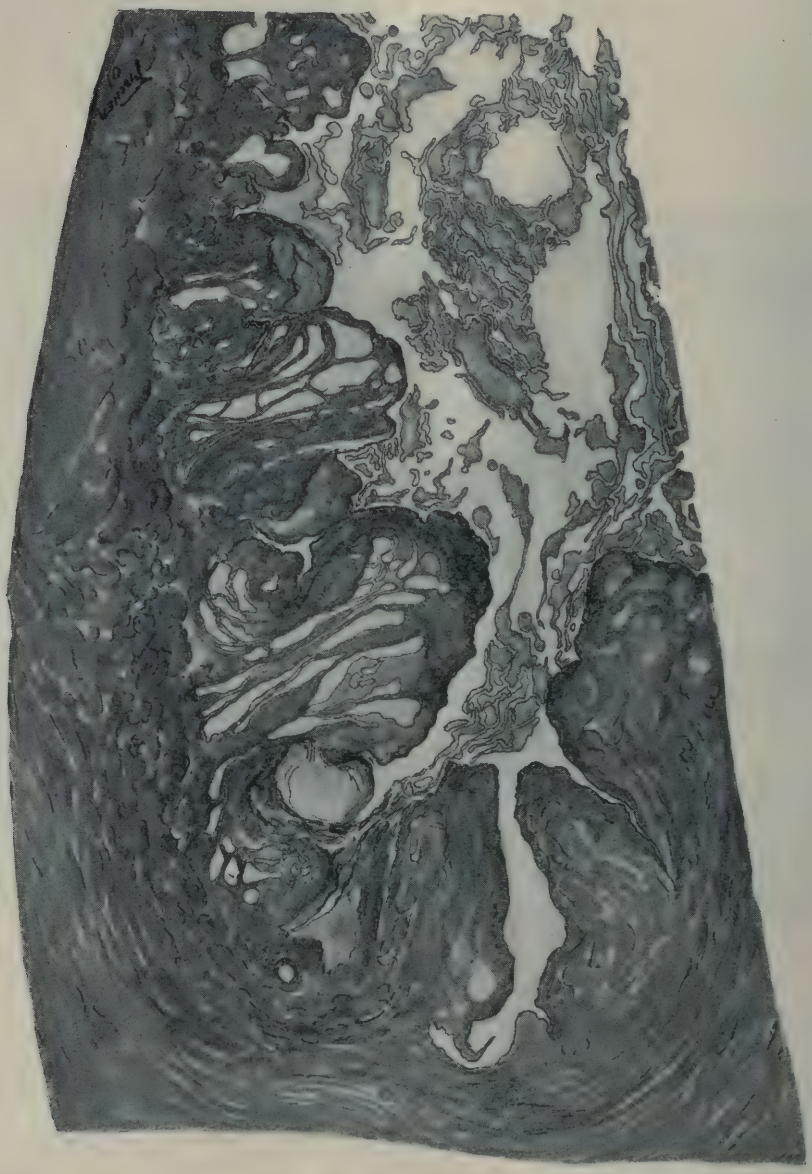


epithelium flattened or cubical. Bloodvessels are intimately associated with the decidual cells, and free blood is found in the decidua and musculature.

Chorionic Villi. It is observed that the intensity of the stain is subject to great variation, particularly in the connective tissue stroma. The larger the villus the fainter is the stain; while in the largest villi the central portion of the stroma utterly fails to take a stain, thereby showing complete degeneration and loss of tissue. At the periphery of the villus, where the stroma seldom if ever is wholly lost, there is a faint stain, showing but partial degeneration. This is best shown by the Van Gieson stain. Great variations in staining are also shown in the epithelial layer, the cells lying nearest the stroma taking the stain

more faintly than those at the periphery. The non-degenerated connective tissue of the villus is of the embryonal type; the cells are elongated, having spindle-shaped nuclei. There is not the degree of development into fibrillæ as described by Webster[18] in the chorion of the fourth month, but it resembles in point of development the villus

Fig. 2.



of four to six weeks' development. The first evidence of degeneration in the connective tissue is shown in the indistinct outline of the cell body, which becomes a granular substance beset with stellate cells containing a granular nucleus, and from which radiate fine fibrillar processes. Finally the formed elements disappear, and there is left an irregular space filled with clear serous fluid. At the periphery, in

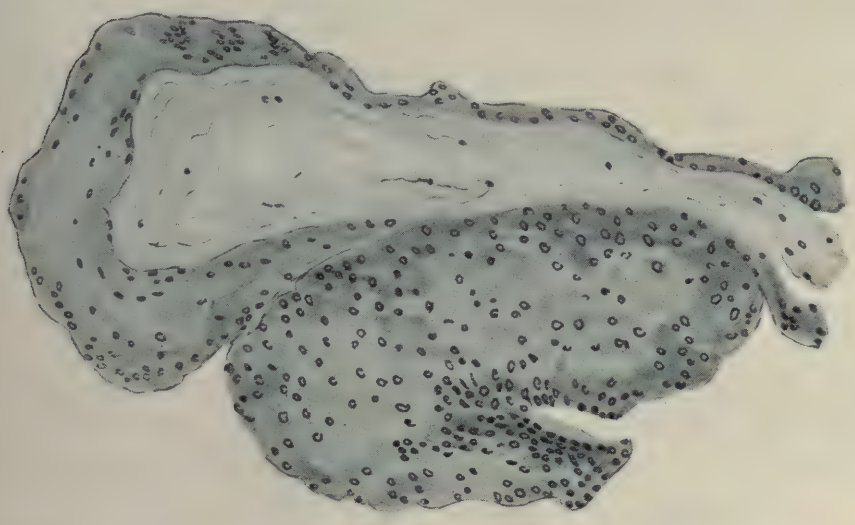
close touch with Langhans' layer, there always remains more or less connective tissue, arranged in concentric layers, which is more fibrillar than that of the centre of the stroma. In none of the villi is the stroma wholly degenerated. The degeneration of the stroma is in

FIG. 3.



direct proportion to the size of the villi; in the smaller villi there is little if any degeneration. The process seems to be a granular degeneration or necrosis, with subsequent absorption, leaving spaces which fill with serum. I have not been able to demonstrate mucoid degeneration, as was first affirmed by Virchow. Storch took issue with Vir-

FIG. 4.



chow on this point, and, after him, the lesion is spoken of as "cystoid degeneration of Storch." Other authorities, while agreeing with Storch, disagree as to the manner by which this "cystic degeneration" is brought about. Merkle and Giese call it a secondary œdema due to an inhibited formation of the placenta. Koster and Rumler believe

it to be an œdema of the stroma resulting from interference with the circulation through the pedicle of the vesicle.

Kreutzmann[19] also takes issue with Virchow. He says: "Vesicular mole is the result of an irregular proliferation of the epithelial parts of the chorion, with hydropic swelling and consecutive necrosis, manifested especially in the larger vesicles. The superficial stratum of the stroma—that which is near the living epithelium—remains unchanged, but the inner parts become liquefied."

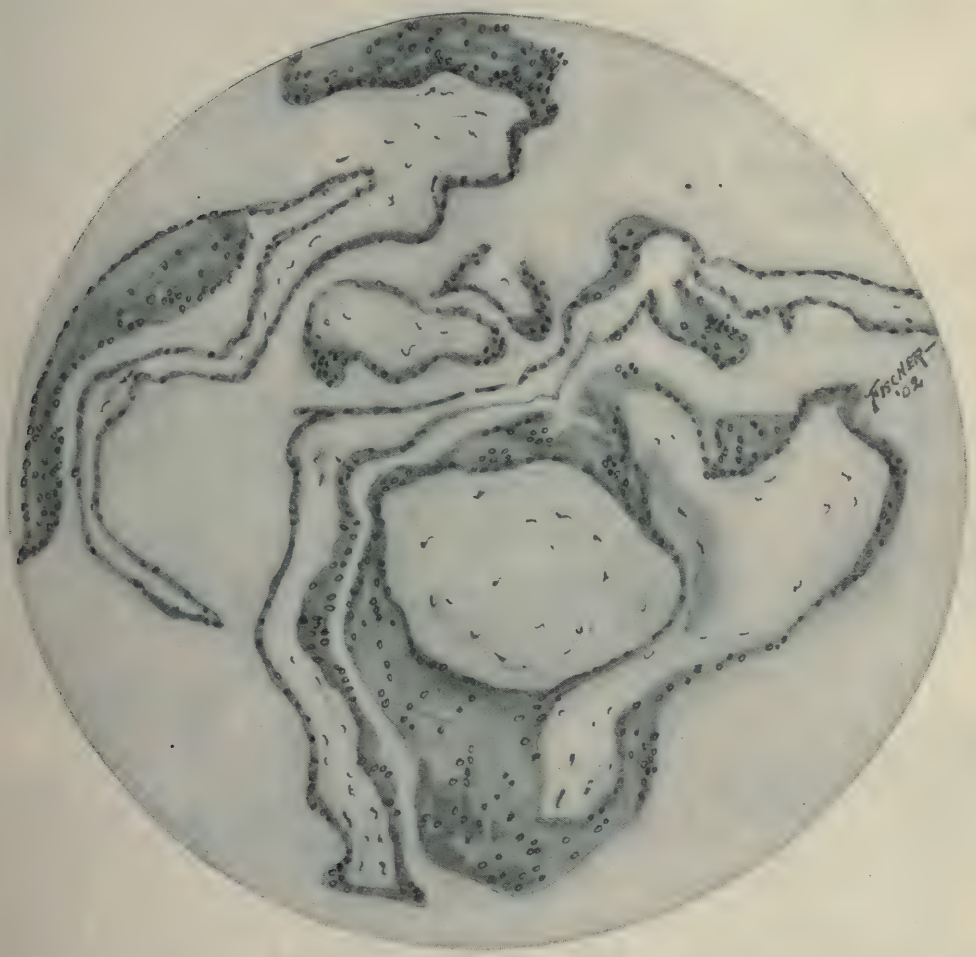
In addition to the above-named authorities may be mentioned Marchand, Fraenkel, and Neumann, who believe in the cystic degeneration theory as opposed to the myxomatous degeneration theory of Virchow. They speak of the proliferation of the epithelial elements as being coincident with the liquefaction of the stroma.

Bloodvessels in the villi are difficult to demonstrate. Webster in describing the chorion of the sixth week of development says: "Most of the villi have capillaries. These consist simply of a tube of small, flat, endothelial cells around which the connective tissue is somewhat condensed, though to a different extent in various places." No bloodvessels were seen in the large cystic villi; and when seen in the small, less degenerated villi they appear thicker-walled than is described by Webster (*vide supra*). No calcareous deposits were seen in the villi. The most significant changes centre in the epithelial elements of the chorion. There is seen an active and very irregular proliferation of the epithelial cells, with a tendency to invade the uterine structures to a degree not seen in normal pregnancy. Before degenerative changes are noted in the stroma the epithelial layers proliferate to an unusual degree. This proliferation of epithelium is particularly marked at the tips of the villi. The larger the villi the greater the proliferation. This proliferation, while similar in character, is to a greater degree than is found in normal pregnancy of the same age, and may surpass that found at any time of pregnancy.

In the syncytium and Langhans' layer of the small villi there is little change from the normal. As the villi enlarge through degenerative changes in the stroma and proliferation of the epithelial elements there are seen in the periphery of the villi, particularly at the distal end, clumps and buds of protoplasmic bodies taking a deep stain and containing irregular groups of nuclei. Irregular vacuoles are seen in these protoplasmic bodies. The protoplasm is finely granular, and takes a fainter stain than do the nuclei. The buds and clumps of protoplasm take a deeper stain than do the remaining portions of the epithelium. Here and there in the larger villi irregular nests of syncytium are seen in the stroma of the villi. These, according to Van der Hoeven, are *prima facie* evidence of malignancy. A careful study of my specimens relative to this phase has led me to the conclusion that such is often,

though not always, an accidental finding, due to tangential cutting of the villus, and not to an active invasion of the stroma by the epithelial elements. These changes in the syncytium and Langhans' layers are essentially hyperplasia and necrosis of the cell elements; the protoplasm increases in amount and the nuclei in size and number. The vacuoles are in number and size directly proportionate to the amount of epithelium, and are doubtless due to degenerative changes from malnutrition. Coagulation necrosis of the syncytium is more or less in evidence

FIG. 5.



throughout the specimen. With the death of the fœtus there is loss of the fœtal blood supply to the villi. This does not necessarily result in necrosis of the villi, providing the maternal blood supply is sufficient to provide the needed nourishment; on the contrary, the villi may continue to grow.

According to Marchand, the fœtal blood is of minor importance in supplying nourishment to the villi. As evidence of this he has demonstrated necrosis of the stroma in the presence of a fœtal blood supply and in the absence of a syncytial covering. His conclusion is that the

syncytium exercises a governing influence over the maternal blood supply to the stroma of the villi; when destroyed the stroma will undergo degenerative changes. Marchand asserts that well-formed stroma is found only where the maternal circulation is adequate and the syncytium intact.

It is found that in partial moles where the maternal circulation is less disturbed the necrosis of the stroma is correspondingly less. It would appear, then, that the remote cause of the necrosis of the chorion lies in the failure on the part of the maternal circulation leading to degeneration of the connective tissue, and to a serous exudate which finally replaces the stroma of the villi. Peters[20] believes the syncytium to be a sort of endothelial layer lining the intervillous spaces and exercising some important part in the function of interchange between maternal and fœtal circulation. Furthermore, that it serves to protect the maternal blood from direct contact with Langhans' layer, which probably has some coagulating or destructive influence on the maternal blood.

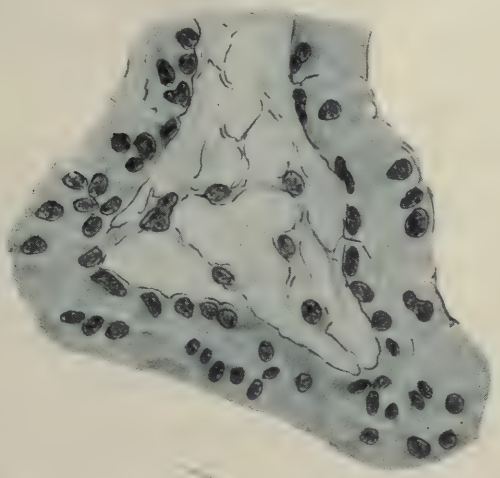
With a disturbance of the maternal circulation the reciprocal relations between the maternal and fœtal circulation is altered, and, as a result, there is added to necrosis of the stroma a serous exudate, with the formation of cystic spaces, filled with clear serum. The accumulated fluid in turn causes further necrosis of the stroma through compression; complete degeneration of the connective tissue fibres is seldom if ever seen. There is always a limited amount of fibres compressed in a concentric manner immediately beneath the Langhans' layer. In the larger villi there is also pressure necrosis of the epithelial covering, affecting both Langhans' layer and the syncytium.

Malignant Degeneration of Hydatiform Mole. The greatest interest in hydatiform moles centres in the fact of their liability to undergo malignant degeneration. Solowij and Krzysz-Kowski[21] have shown that about 10 per cent. of hydatiform moles become malignant. On the other hand, it is generally recognized that fully 40 per cent. of the cases of syncytioma malignum arise from hydatiform mole. In collecting reported cases of hydatiform mole I have found a scarcity of case-reports of non-complicated hydatiform mole; that cases are seldom reported unless they have undergone malignant degeneration. For this reason it is impossible to arrive at any exact estimate of the frequency of hydatiform moles and of their malignant degeneration. Referring to the following table of reported cases, which includes all I am able to find in the literature, it appears that 16 per cent. of hydatiform moles become malignant. For the reason stated above it is probable that this percentage is far too high.

From the very onset the difficulties involved in dealing with the many mooted questions concerning the malignancy of hydatiform mole

appear insurmountable. The intimate blending of fœtal and maternal structures, together with the secondary processes of degeneration, are so complicated and are so subject to variations that it is difficult and at times impossible to distinguish the benign from the malignant. Indeed, Van der Hoeven[22] goes so far as to state that all hydatiform moles are malignant; that the proliferation of the epithelial elements of the chorion (syncytium, Langhans) assumes a malignant type in the invasion of the uterine musculature and connective tissue stroma of the villi. He further reasons that if this tendency on the part of the epithelial elements to proliferate is not marked, or if the mole is expelled or removed before the epithelium invades the uterine tissue beneath the line of cleavage (within the compact layer of the decidua), there can be no recurrence. If left behind in the uterine tissue the epithelial elements continue to proliferate and to be carried to distant parts

FIG. 6.



of the body by way of the blood stream, there forming metastatic malignant epithelial growths.

Neumann[23] studied 8 cases of hydatiform mole; 5 were not followed by malignant changes, 3 died of syncytioma malignum. In the 5 so-called benign moles the epithelium of the chorion proliferated to an unusual degree, but did not invade the connective tissue of the stroma, while in the 3 malignant moles the connective tissue stroma was invaded by syncytial giant cells. Neumann arrived at the conclusion that the earliest evidence of malignancy lay in the invasion of the connective tissue stroma of the villi by the epithelial elements of the chorion. As suggested by Pierce,[24] the "view of Neumann is not generally recognized, and with right, for cases of nephritis and lead poisoning have since been described where the same cells were found in the stroma of normal villi; hence their presence can have no pathological significance in hydatiform mole."

It is evident from the observations of Veit,[25] Webster,[18] Pick,[27] and others that the invasion of the deep structures of the uterus, and even of structures beyond the uterus, by chorionic epithelium, is not evidence *per se* of malignancy; that, on the contrary, syncytial masses are found in the uterine musculature, and are deported to distant parts of the body by veins in normal pregnancy; that soon after the termination of pregnancy they disappear. The transition between benign and malignant chorio-epithelial elements is a gradual and imperceptible one, just as is true in the transition of all benign hyperplastic growths into the malignant types; and to differentiate them is manifestly impossible. There undoubtedly exists an intermediate stage between the benign and malignant. Berry Hart examined a hydatiform mole in which the epithelial changes were identical with those described in the malignant type; no recurrence followed the expulsion of the mole. Both the syncytium and Langhans' cells participate in the proliferative changes, but to a varying degree. There is, likewise, great variation in the rate of growth in the epithelial elements, the explanation not only lying inherent within the cell elements, but also in the degree of resistance offered by the uterine tissue.

Two of the cases described by Kworostansky[26] were in the second month of pregnancy—one a benign hydatiform mole, the other a syncytioma malignum. It is of the greatest interest to compare these two cases from an anatomical point of view. In the benign mole there was unusual proliferation of the syncytium and Langhans' layer, forming a loose connection with the decidua serotina; in the veins of the serotina both syncytial and Langhans' cells were found in limited numbers. The decidua vera was invaded to a lesser degree; no epithelial elements were found in the uterine musculature. In the placental site were evidences of endometritis, as demonstrated in scrapings removed six weeks after the expulsion of the mole. The case recovered without recurrence. The author states that the patient, aged twenty-four years, was anæmic, and that this impoverishment of the blood afforded insufficient nourishment to the villi, thereby exciting the chorio-epithelioma to extend deeper into the uterine musculature in order to obtain greater nourishment. Sufficient nourishment not being provided by the stroma of the villi, necrosis follows. In the second case, which was malignant, there was also extreme anæmia. The epithelial elements behaved similarly to that of the first case, only to an exaggerated degree, apparently differing only in the degree of epithelial invasion of uterine structures. The syncytial cells invaded the intermuscular spaces and veins of the uterus as far as the parametrium. Atrophy and necrosis of the decidual and muscular elements followed; bloodvessels were changed to blood lacunæ.

In comparing my specimen of benign hydatiform mole with one

having undergone malignant changes, it was advisable to select for comparison not only one of similar age, but also one that had been removed togther with the uterus, as was mine. In this way we avoid certain retrogressive changes and the disturbance of anatomical relations which would otherwise mislead. Two such cases have been reported—one by Poten and Vassmer, the other by Neumann.[23] In both these cases the essential variation from my own case appears to lie in the more marked proliferation of the syncytium and Langhans' cells and in their extended invasion of the uterine veins and musculature. While it is not to be expected that a benign mole may be recognized from a malignant mole by the naked eye, yet it is worth while to observe that Pautz[28] and others have found in malignant moles that the villi rarely attain large size, are firm, and have a long, slender pedicle, giving to the mole the appearance of soft, cooked rice.

Ladinski,[31] in a recent clinical review of deciduoma malignum, reported a case of hydatiform mole followed by malignant degeneration (reported too late to be inserted in the accompanying tables). He collected thirty-three similar cases, and concluded that malignant degeneration occurred most frequently in cases where mole pregnancy terminated in the fourth month. It does not appear that the length of time that a mole remains *in utero* has any influence upon its disposition to become malignant. In twenty cases Ladinski finds the average time of appearance of syncytioma malignum is eight weeks after the mole has been expelled.

Diagnosis. The rate of growth of the uterine tumor is the most constant and characteristic sign of hydatiform mole. With few exceptions, the size of the uterus is greater, even to double that of the normal pregnant uterus of a like period. At twelve weeks it has been found larger than the average pregnant uterus at full term. The growth is not usually symmetrical; in a number of cases the uterus is found to be proportionately broad. Furthermore, the rate of growth is not uniform. Near the time of expulsion the uterus frequently assumes a very rapid growth, soon to be followed by uterine pains and profuse hemorrhage. Within twenty-four hours the uterus may ascend two or three fingers' breadth.

Hemorrhage is usually the first symptom to attract the attention of the patient. Preceding the hemorrhage is a period of amenorrhœa extending over one, two, or three months—rarely longer. In a single case hemorrhage appeared in the third week of gestation, and again as late as the fifth month. The usual time of occurrence is in the second and third months. It is occasionally stated that the hemorrhage is more profuse at night. This was true in my first case, there being very little loss of blood during the day and profuse bleeding at night. As a rule, the hemorrhage is at first slight, gradually

increasing in amount and frequency, finally becoming continuous and in such quantities as to cause more or less anæmia. Hemorrhage is always to be feared at the time of the expulsion of the mole; this is particularly true when the mole is far advanced and when firmly adherent to the uterus. It has been known to recur within a week in a case that did not prove to be malignant, but such an event is exceptional. Where malignant degeneration has followed the birth of a mole hemorrhage is known to have recurred nine days after the mole was expelled, and as late as four and one-half years. Consulting the accompanying tables, it is seen that hemorrhage, ushering in malignant changes, first appears in the first and second months, with about the same frequency as in the fifth and sixth months following the expulsion of the mole. We may formulate the dictum that hemorrhage

FIG. 7.



recurring weeks and months after the expulsion of a hydatiform mole is suggestive of malignancy, and demands immediate and thorough investigation into the cause.

Nausea and vomiting are present in a larger percentage of cases than is common to pregnancy. Severe and uncontrollable vomiting occurred 18 times in the 210 collected cases. The explanation probably lies in the unusual distention of the uterus.

Pain in the back and pelvis is complained of in nearly all cases, but does not usually develop until hemorrhage has persisted for some time. Not infrequently pain is absent until the hemorrhage is profuse and the cervix dilating.

In extensive degeneration of the chorion the fœtus dies early and is absorbed. We then have none of the physical evidences of a fœtus. In partial degeneration of the chorion the development of the child

may not be hindered, and there may be no clinical evidences of vesicular degeneration.

The consistency of the uterus is a subject of some importance from a diagnostic point of view. Poten reported eleven cases of hydatiform mole, in three of which he observed irregular contractions of the uterine wall. These contractions were localized over a limited area, and were transient, lasting but a few minutes and reappearing at variable intervals. To the examining finger they might easily be mistaken for intramural fibroids. Poten does not claim this is a reliable sign, but suggests that further investigation of the phenomena be made.

An early diagnosis of hydatiform mole is of importance because of the liability to malignant degeneration. While, as a rule, there will be the usual clinical signs of a mole some time before malignant changes develop, there is always the possibility of early malignant transformation, and it is not possible to detect these early malignant changes. Our only safeguard lies in the early recognition of the mole and in its immediate removal.

Will the microscope supply an infallible means of making an early diagnosis of malignant degeneration of the mole? We do not accept the statement of Van der Hoeven and Neumann that epithelial invasion of the stroma of the villi is the earliest and at all times reliable evidence of malignancy. As has been stated, such findings are not uncommon in normal pregnancy. Marchand failed to find the stroma invaded in a malignant mole, and Ruge found such invasion in an undoubted benign mole. In my second case there was epithelial invasion of the stroma of the villi. Two years have elapsed since the removal of the mole, and no sign of malignancy has developed.

In a case reported by Poten the mole went on to the time of full-term pregnancy. Neumann's cells were found in the stroma of the villi. On the twenty-sixth day after the mole was expelled hemorrhage recurred to a slight degree. The uterus was curetted, and a microscopic examination of the scrapings showed no evidence of malignant invasion; recovery followed. This case shows how difficult, and at times impossible, it is to determine the character of a hydatiform mole. In the light of our present knowledge we must always make a guarded diagnosis in the early stage; and at no time can a diagnosis be made with absolute certainty from the expelled mole. The invaded decidua, and if possible the underlying musculature, will alone afford evidences of malignant invasion prior to the development of metastasis. In the case reported by Schmidt a diagnosis of malignancy was first made from a microscopic examination of a metastatic growth which appeared in the vagina. The uterus was not removed, and recovery followed the removal of the vaginal growth. When hemorrhage recurs

days or weeks after complete removal of the mole the uterus should be curetted and the scrapings examined for active and extensive invasion of the uterine tissues. Large nuclei, rich in chromatin and mitotic figures, together with a tendency on the part of the protoplasm to separate into individual cells or chains of cells, is, according to Voigt and Gottschalk, suggestive of malignancy.

We are forced to the conclusion that as yet we have no certain means of making an absolute and early diagnosis of malignant degeneration of a hydatiform mole. The clinical signs, together with the gross and microscopic appearances, are all to be carefully considered. In view of our inability to make an absolute early diagnosis, vesicular degeneration of the chorion, however limited, demands immediate interference, to be followed by a period of at least three years of watchful expectancy; and if, at any time following the expulsion of the mole, hemorrhage recurs, the uterus is to be curetted and a microscopic examination made of the scrapings.

Prognosis. Regarding the prognosis of hydatiform mole, experience teaches us to look with suspicion upon all cases, even months and years after the removal of the mole. It is seldom that serious consequences occur while the mole is *in utero*. Malignant degeneration, rupture of the uterus, fatal hemorrhage—all these have occurred with the mole *in situ*, though such happenings are, fortunately, rare. We have learned to fear remote results—*i. e.*, a repetition in subsequent pregnancies and malignant degeneration of retained chorio-epithelium. Heitzman estimated the mortality at 13 per cent. These statistics were gathered at a time when chorio-epithelioma malignum was not recognized. It is generally accepted that 10 per cent. of hydatiform moles undergo malignant degeneration. This estimate is generally accepted as approximately expressing the death rate of hydatiform mole; but it is far too small, as shown by the following data deducted from the accompanying tables. Death from hemorrhage and, to a lesser degree, from septic infection and rupture of the uterus add materially to the death rate, bringing the mortality to near 25 per cent.

In the 210 cases here recorded there were 49 deaths—a mortality of about 25 per cent. Of this number 32 died of syncytioma malignum (16 per cent.), 7 died from hemorrhage (4 per cent.), 4 died of septic peritonitis (2 per cent.), 1 died of general sepsis, 1 from uræmia, 1 from endocarditis and nephritis, one from meningitis, and 2 from unknown causes. The author does not regard these statistics as expressing actual facts. There is doubtless a tendency to report all cases resulting fatally and to overlook those having no special point of interest in their course and termination.

The later in pregnancy we have to do with vesicular degeneration of

the chorion the more grave the prognosis, because of the difficulty in removing the mole—the greater liability to rupture of the uterus and to malignant degeneration. It has been stated, and it will bear repetition, that the removal of a hydatiform mole is imperative as soon as the diagnosis is established. There can be no temporizing, however limited the vesicular degeneration and however early or late the condition is recognized. Where but a small area of the placenta is involved the diagnosis is not made until the termination of pregnancy; hence the question of interference will not arise during pregnancy, but the same degree of watchful expectancy must be exercised after the ter-

FIG. 8.



mination of pregnancy. While all agree as to the disposition that shall be made of the mole, it is always a grave question as to what shall be our attitude toward the uterus after the mole is expelled. Solowiz[21] has advised hysterectomy in all cases, and surely this would be the logical conclusion were we to agree with Van der Hoeven that all hydatiform moles are malignant.

Recognizing the frequency of malignant degeneration of hydatiform mole, and finding our most reliable and early evidences of malignant invasion in the decidua, we indorse the advice of Butz, who would curette the uterus ten or twelve days after the expulsion of the mole, for the purpose of removing remaining fœtal elements and of making a microscopic examination of the scrapings to detect a possible malig-

nant invasion, as shown by active proliferation by the chorio-epithelium. Doubt will occasionally arise after such a procedure, and where such doubt exists the uterus should be removed on suspicion.

Respecting the influence of hydatiform mole upon future childbearing, it is observed that healthy children are born subsequent to the expulsion of the mole, and that there does not appear to be acquired an added tendency to abortion. Contrary to the statement made by most text-books, it is the exception for a woman to give birth to more than one mole. In the 210 cases but two women gave birth to two moles, one to four (not recorded), one to five (not recorded), and one to eleven. It is furthermore seen that conception is possible very soon after the expulsion of the mole. On the other hand, a period of twenty years of sterility, and in two instances ten years, have preceded the development of the mole. It is correctly stated that multipara are more liable to hydatiform mole than are primipara. In the 210 cases 42 were primipara, 139 multipara, and 29 not recorded.

Treatment. Since we are ignorant of the essential and predisposing causes of hydatiform mole, no prophylactic measures can be instituted. In not a few of the reported cases, where hemorrhage was severe and even threatened the life of the patient, prior to the expulsion of the mole the attending physician resorted to vaginal tampons to check the hemorrhage, and at the same time administered ergot. The hemorrhage has in this manner been controlled, and not infrequently the uterus has been made to contract and expel the mole. By reference to the accompanying tables it will be seen that transfusion was made where hemorrhage had caused collapse either before or after the expulsion of the mole.

In all cases the mole is to be removed by the finger and placental forceps, only resorting to the curette when it is found impossible to remove the placental tissue by the finger and placental forceps. In the following reports of cases I have noted that the curette has often been used to remove the mole and as an aid to the finger in cleaning out the uterine cavity after the expulsion of the greater portion of the mole. In the cases where hemorrhage continued after the expulsion of the mole the bleeding was checked by curettage. While in no case was there an apparent bad result from the use of the curette, it is evident that the dangers of perforating the uterus must be great, because of the overdistention and weakening of the uterine wall by invading placental tissue. Too great caution and conservatism cannot be used in the employment of the curette.

When the mole is expelled spontaneously it is imperative to explore the uterine cavity with the finger, to make sure that all placental tissue has been removed. After the expulsion of the mole the patient should be under the supervision of a physician for a period of not less than

three years, during which time occasional bimanual examinations are to be made. The possibility of metastatic growths arising must be borne in mind. All suspicious new-growths in the vagina are to be removed for microscopic section, and all disorders of the lungs are to be regarded with suspicion, fearing metastatic invasion. Hemorrhage from the uterus at any time during the period of watchful expectancy demands an exploratory curettage and microscopic examination of the scrapings. Where there is unmistakable evidence of malignant invasion of the uterine tissue, or where there is a reasonable doubt as to the true nature of the invading epithelium, no time should be lost in performing hysterectomy. It happened with Shauta, as well as in my own case, that hemorrhage was so great in the attempt to remove the mole that hysterectomy was resorted to. In my own case the general clinical signs suggestive of malignancy, the near approach to the climacteric, and the presence of bilateral ovarian cysts gave added support to the radical procedure.

SUMMARY. 1. Nothing definite is known of the immediate and remote causes of hydatiform mole. It most frequently occurs between the ages of twenty and thirty, and is two and one-half times as frequent in multipara as in primipara. Neither general nor local disease is positively known to have a direct bearing upon the development of the mole.

2. The weight of evidence is in favor of a maternal origin, the vesicular degeneration of the chorionic villi resulting from a disturbed maternal circulation. Failure on the part of the maternal circulation causes a degeneration of the connective tissue stroma of the villi, together with serous infiltration or œdema. The syncytium and Langhans' cells penetrate deeper into the decidua, where the nutrition is adequate—a fact which accounts for the unusual proliferation of these epithelial elements in hydatiform mole.

3. There is no proof that cystic degeneration of the ovaries has any influence upon the development of cystic degeneration of the ovum. The former is so common as compared to the latter that it is not likely they stand in relation of cause and effect.

4. Malignant degeneration of hydatiform mole occurs in about 16 per cent. of all cases. No sharp line can be drawn between benign and malignant hydatiform moles. Syncytial invasion of the connective tissue stroma of the villi and of the uterine musculature occurs under normal conditions, and cannot be regarded, in hydatiform mole, as evidence of malignancy unless found to a marked degree.

5. It follows that a macroscopic and microscopic examination of discharged vesicles will not determine the benign or malignant character of a mole.

Hydatiform Mole.

Case No.	Age	Children.	Abortions.	Puerperium.	No.	Age.	Symptoms and course.	Duration of sympts.	Termination.	Remote results.	Reference.	Remarks.
1	21	0	0	.....	1	8–10 weeks.	Hemorrhage; rapid growth of uterus; uncontrollable vomiting.	24 days.	Induced.	Death from septic peritonitis.	I. Edgar.	Septic infection started from the lacerated cervix.
2	24	3	1	Normal.	1	12 wks.	Hemorrhage began tenth week; no pain.	2 wks.	Induced.	Recovery	Kworostansky, Arch. f Gyn., 1901, lxii.	Hemorrhage returned in one week, curettement was followed by recovery
3	25	2	0	"	1	.....	Began with hemorrhage 10th week.	10 wks.	Spontaneous.	"	Poten, Monat. f. Geb., xiv. 43.	At 4½ months uterus was one finger breadth above umbilicus.
4	47	0	0	.....	1	12 mos.	.....	.....	"	"		
5	22	0	0	.....	1	8 wks.	.....	.....	"	"	Ibid.	Uterus at level of the umbilicus.
6	29	5	0	Normal.	1	.....	Recurring hemorrhage.	.....	Induced by finger.	Decidu-oma malig.	Schauta, Cent. f. Gyn., 1895, 248.	Watery fluid continued to escape after removal of mole; two weeks later hemorrhage returned.
7	40	4	0	"	1	.....	Hemorrhage began in fourth month.	.....	"	"	Pick, Berl. Med. Woch., 1897, 1070.	Malignant growth in vagina found while mole was in utero.
8	22	...	...	.....	1	4 mos.	Hemorrhage.	.....	Spontaneous.	"	Ibid.	Malignant growth in vagina; mole was apparently benign.
9	23	1	1	Normal.	1	3 mos.	Hemorrhage.	3 wks.	"	"	Tannin, Arch. f. Gyn., 1895, 94.	Hemorrhage returned five months after mole was expelled.
10	36	8	0	"	1	40 wks.	Uterus slightly larger than normal.	.....	"	Recovery	Poten, Monat. f. Geb., xiv. 3.	Mole ceased to grow during last month; when expelled it showed degenerative changes; this speaks against Van der Hoeven's theory of malignancy of all hydatid moles.
11	32	5	0	"	1	5 mos.	Hemorrhage began in 5th week; uterus at level of umbilicus end 4th mo.	19 wks.	Induced.	"	Ibid.	
12	30	2	0	.....	1	.....	Uterus size of full-term pregnancy; œdema of feet; albuminuria.	.....	Hysterectomy.	"	Ibid.	Double ovarian cyst.
13	23	4	2	Normal.	1	10 wks.	Hemorrhage and pelvic pain began in 9th week.	8 wks.	Induced.	Decidu-oma malig.	Gebhard, Zeit. f. Geb., xxxvii. 480.	Hemorrhage returned fourteen days after mole was removed; hysterectomy done one week later.
14	42	9	0	"	1	16 wks.	Hemorrhage and pelvic pain began in 8th week.	8 wks.	"	Recovery	v. Franque, Zeit. f. Geb., xxxiv. 199.	

15	41	...	...	.....	1	7 wks.	Began 13th week to bleed profusely.	6 wks.	Spontaneous.	Syncytioma malig.	Schmidt.	Metastatic growth found in vagina in thirteenth week of pregnancy; *uterus was normal and remained so;* first proliferation of epithelium of chorion travelled by blood stream to perivaginal tissue; recovery after removal of vaginal growth, uterus not removed; probably recovery due to early removal; mole in utero may have been malignant, but expelled.
16	26	...	...	.....	1	.....	.....	.....	.....	.....	R. Winkler.	Became malignant one year after expulsion of mole; metastasis in lungs.
17	22	1	0	Normal.	1	About 16 wks.	Sudden profuse hemorrhage; no pain; bleeding lessened; uncontrollable vomiting at this time (about middle 4th mo.); later sudden profuse hemorrhage.	13 days.	Induced.	Syncytioma malig.	Inglis.	Followed by cerebral hemorrhage six months later. Post-mortem found syncytioma of left occipital lobe similar to syncytial masses found in uterus.
18	42	7	0	"	1	4 wks.	Sudden flowing, with clots, followed by abdominal pain and some vesicles; three w'ks later she again bled profusely.	3 mos.	Induced (curette).	"	Buist.	Hemorrhage returned nine days later; curetted and carbolic acid applied; returned again in a few days, and a month later hysterectomy; syncytioma found in uterus; left ovary cystic.
19	51	8	1	"	1	.....	Sudden profuse bleeding.	8 wks.	Spontaneous.	"	Buschbeck.	Mole preceded by one year of amenorrhœa; after expulsion hemorrhage recurred at frequent intervals; soon a fetid blood discharge followed.
20	35	3	...	"	1	.....	" " "	2 wks.	Induced.	"	Kruser.	Endometritis present; metastasis of right lung.
21	28	4	1	"	1	4 mos.	Sudden profuse bleeding following partial abortion.	2 mos.	"	Recovery	Madden, Trans. Roy. Acad., Ireland, 1888, vi. 295.	Mole remained in uterus two months, then removed by curette; hemorrhage continued throughout the two mos.
22	30	8	0	"	1	7 mos.	" " "	.....	"	"	Ibid.	Miscarried at seventh month; mole partially retained six months; very anæmic.
23	39	8	...	"	1	7 mos.	Hemorrhage slight in 4th and 5th month.	4 mos.	Spontaneous.	"	Triffith, Sr., Obst. Soc., London, 1888, 82.	
24	35	...	...	.....	1	.....	Swelling of ankle and legs; flooding in 5th mo.	.....	"	Death.	Ross, Brit. Med. Jour., 1898, p. 1814.	No autopsy.
25	29	2	0	Normal.	1	4 mos.	Hemorrhage in 3d mo.	.....	Induced.	"	Lamaestre, Bul. de la Soc. Anat., 1846–47, 326.	
26	26	1	...	.....	1	.....	Hemorrhage.	.....	Spontaneous.	"	Hooker, Bost. Med. and Surg. Journ., 1837, 91.	Hydatids weighed 6 or 7 lbs.; death due to peritonitis; condition of ovary not stated.
27	33	5	0	.....	1	.....	"	.....	"	Recovery	Haines, Dublin Quart. Journ., 1850, 201.	Subsequent portion of mole expelled two weeks later.

Case No.	Age	Children.	Abortions.	Puerperium.	No.	Age.	Symptoms and course.	Duration of sympts.	Termination.	Remote results.	Reference.	Remarks.
28	28	...	...	.....	1	.....	Hemorrhage in 3d mo.	.....	Induced.	Recovery	Hewitt, Lancet, 1862, 369.	Uterus above umbilicus end of third month.
29	25	2	...	.....	1	2 mos.	"	.....	"	"	Hutchinson, Ibid.,1851, 411.	
30	27	2	...	.....	1	.....	"	.....	"	"	Jamison, Ibid., 1867, 259.	
31	23	2	...	.....	1	.....	"	.....	"	"	Hunter, Ibid., 1846.	Living child born; portion of placenta degenerated.
32	30	2	1	.....	1	.....	Uncontrollable vomiting; hemorrhage 2d month.	.....	"	"	Harrington, Clin. Rep., Chicago, 1878, 387.	
33	29	...	1	.....	1	.....	Hemorrhage 2d month; persistent nausea and vomiting.	.....	"	"	Humphrey's Chi. Med. Journ., 1878, 176.	
34	30	2	...	.....	1	3 mos.	Hemorrhage 5th week; vomiting severe.	.....	Spontaneous.	"	Jackson, Bost. Med. & Surg. Journ., 1864, 138.	Well-developed fœtus; cord and large portion of placenta normal.
35	47	11	0	Normal.	1	10 wks.	Continuous hemorrhage, pelvic pain; cachexia.	.....	Induced.	Death from septic infection.	Solowy & Kryzkowski, now Gekarskie, 1900, Nos. 22 and 28.	Last pregnancy five years prior to expulsion of mole.
36	38	7	0	"	2	.....	Hemorrhage.	.....	.....	Deciduoma malig.	Lonnberg and Mannsheimer, Monatsch. f. Geb., 111.	Hydatid mole expelled three years previous; healthy child born later, then followed second mole.
37	48	8	2	"	1	9 wks.	"	.....	.....	"	Bacon, Amer. Journ. of Obst., 1895.	Hemorrhage returned five months after mole was expelled; metastasis in broad ligaments and lungs.
38	42	2	0	"	1	4 mos.	.....	.....	.....	"	Pestalozza, Centrl. f. Gyn., 1896, 175.	The uterine musculature was penetrated by the mole.
39	42	2	0	"	1	.....	Hemorrhage.	5 mos.	Spontaneous.	"	Apfelsted and Aschoff Arch. f. Gyn., l. 515.	Died from metastasis.
40	40	3	0	.....	1	.....	.....	.....	.....	"	Neumann & Schanta, Centrl. f. Gyn., 1896.	Nodule in vagina during pregnancy; cystic degeneration of both ovaries; metastasis in lungs.
41	44	2	0	Normal.	1	8 wks.	Irregular hemorrhage.	2 mos.	Spontaneous.	"	Lindfors, Centrl. f. Gyn., 1896, 6.	
42	33	5	0	"	1	.....	Hemorrhage.	.....	Induced.	"	Scherer, Arch. f. Gyn., lvi.	Hemorrhage returned fourteen days after mole was expelled; metastasis in lungs, liver, and brain.
43	43	12	4	"	1	5 mos.	.....	.....	"	"	Zondrk, Zeit. f. Geb., xxxvii. 157.	Hemorrhage returned in two weeks; hysterectomy, recovery.
44	23	...	...	.....	1	.....	.....	.....	"	"	Gebhard, Zeit. f. Geb., 1898, 39.	Hysterectomy three weeks after mole was removed.

45	52	...	...	.....	...	.....	.....	.....	Induced.	Deciduoma	Holleman, Diss., Geiden, 1897.	Malignant degeneration two and a hal years after the mole was expelled.
46	42	5	...	Post-part. hem'ge in last birth.	1	3 mos.	Hemorrhage.	2 mos.	Spontaneous.	"	Marchand, Zeitsch. f. Geb., 1898, 39.	Profuse hemorrhage three weeks later.
47	22	...	...	.....	...	6 mos.	"	.....	Spontaneous.	"	Ibid.	Six weeks after mole was expelled the hemorrhage returned; cystic degeneration of both ovaries.
48	38	3	0	Normal.	1	.....	"	Several weeks.	"	Recovery	Ancelet, Geb. des Hôp., 1868, 69.	
49	...	4	0	"	1	7 wks.	Hemorrhage began 3d week.	1 week.	"	"	Ancelet, Ann. de Gyn., 1876, 86.	
50	47	0	0	.....	1	.....	Hemorrhage began 4th week.	....	"	"	Ibid.	
51	29	0	0	.....	1	4 mos.	Hemorrhage began 5th w'k, and became profuse.	3 mos.	"	"	Soc. Obst. de Paris, 1888	Patient very weak and anæmic.
52	51	0	0	.....	1	3 mos.	Hemorrhage.	.....	"	"	Journ. des con. Medico-chir., 1841, 192.	At twelfth week the uterus was as large as at full term.
53	20	1	0	Normal.	1	3½mos.	Hemorrhage, œdema of feet, rapid growth of abdomen.	.....	"	Death.	M. Depaul, Mem. de la Soc. de Biol., 1853, 168.	Died from external hemorrhage.
54	...	6	...	.....	1	5½mos.	Hemorrhage began 2d month.	4 mos.	"	Recovery	Care, Dublin Journ. of Med. Sci., 1878, 335.	Mother syphilitic.
55	23	6	0	Normal.	1	.....	.....	.....	Induced.	"	Coe, Obst. Gaz., 1879–80, 58.	Cysts discharged with watery fluid for two months.
56	16½	1	...	.....	1	4 mos.	Severe hemorrhage.	.....	Spontaneous.	"	Cleeman, Amer. Journ. Obst., 1875, 172.	
57	23	0	...	.....	1	.....	Loss of flesh; nausea, vomiting, hemorrhage late.	.....	"	"	Curtin, 731.	
58	51	9	...	.....	1	4 mos.	Hemorrhage.	.....	"	"	Duncan, Obst. Soc., Edinb., 1883, 162.	
59	33	3	1	.....	1	.....	"	.....	Induced.	"	Davis, Ibid., 1861, 177.	Living fœtus, died soon; twin pregnancy with normal placenta.
60	28	1	...	.....	1	4 mos.	Flooding from first; nausea and vomiting severe.	.....	Spontaneous.	"	Dodge, West. Med. Reporter, 1888, 70.	Uterus size of eight mos. at four mos.; has had four healthy children since.
61	21	1	0	.....	1	.....	Hemorrhage very profuse from start.	.....	Induced.	"	Dearing, Chicago Med. Journ., 1886, 112.	Septic infection following expulsion.
62	23	...	...	.....	1	.....	Pain, hemorrhage.	.....	"	"	Davis, Cincin. Lancet-Clinic, 1887, 695.	
63	45	Several.	...	.....	1	.....	Rapidly growing tumor, no hemorrhage.	.....	Spontaneous.	"	Davidson, Canada Practitioner, 1885, 166	Uterus enlarged irregularly.
64	22	0	0	.....	1	3 mos.	Nausea; no hemorrhage.	.....	"	"	Fischel, St. Louis Med. & Surg. Jl., 1881, 196.	
65	...	3	...	.....	1	7 mos.	Hemorrhage.	.....	"	"	Finnell, Buffalo Acad. of Med., 1862–66, 170.	
66	42	13	0	.....	1	3½mos.	Hemorrhage began 10th week.	.....	"	"	Ford, Amer. Jour. Med. Sci., 1868, 159.	

Case No.	Age	Children.	Abortions.	Puerperium.	No.	Age.	Symptoms and course.	Duration of sympts.	Termination.	Remote results.	Reference.	Remarks.
67	36	6	...	.....	1	3½ mos.	Hemorrhage; vomiting severe.	... ..	Induced.	Recovery	Fifield, Bost. Med. and Surg. Jour., 1857–58, 197.	
68	25	...	...	.....	...	6 mos.	Hemorrhage slight.	.....	"	"	Foote, Med. and Surg. Reporter, 1860, v. 349.	
69	45	0	...	.....	1	3 mos.	Sudden flooding; rapid failure of health.	.....	Spontaneous.	Death.	Finnell, New Jer. Med. Rep., 1855. viii. 370.	Death ten days after expulsion of mole; cystic ovaries not recorded in autopsy.
70	29	3	...	.....	1	.....	Alarming hemorrhage.	.....	Induced.	Recovery	Haulgrave, Brit. Med. Journ., 1893, 458.	
71	13	0	...	.....	1	4 mos.	Vomiting severe.	3 mos.	"	"	Dass, Indian Medical Gazette, 1892, 378.	
72	15	0	0	.....	1	4 mos.	Hemorrhage severe	.....	Spontaneous.	"	Ibid., p. 379.	
73	35	10	0	Normal.	1	.....	Hemorrhage.	.....	Induced.	"	Ibid.	
74	27	5	...	.....	1	.....	"	.....	"	"	Pilliet, Nouv. Arch., d'Obst., 1893, 22.	
75	...	...	...	.....	...	.....	Bloody watery discharge	.....	Spontaneous.	"	Earle, Chic. Med. Jour. Exam., 1877, 52.	
76	19	0	0	.....	1	15 wks.	Hemorrhage began 8th week.	3 mos.	Induced.	"	Githens, Peoria Med. Month., 1880–81, 137.	Healthy child after mole.
77	35	1	0	.....	1	.....	.....	.....	.....	"	Hewitt, Trans. C. Obst. Edinb., 1870, 237.	Three hydatid cysts.
78	33	4	0	.....	1	.....	Hemorrhage.	.....	Spontaneous.	"	Ibid., 1860, 112.	
79	24	1	...	.....	1	.....	"	.....	"	"	Ibid., 251	
80	29	1	...	Dystocia.	1	3 mos.	Hemorrhage in 10th week; no pain.	2 wks.	"	"	Godson, Obst. J. G. B. & I., 1878–79, 701.	
81	27	3	0	.....	1	.....	No hemorrhage; rapid growth of uterus.	.....	"	"	Ibid.	
82	27	2	0	Normal.	1	4 mos.	Hemorrhage in 3d mo.	.....	Induced.	Death.	Lamaestre, Bul. de la Soc. Anat., 1846–47, 326.	Abdomen as large in three months as is the rule in eight months; death from hemorrhage.
83	34	4	0	"	1	6 wks.	Hemorrhage.	.....	Spontaneous.	Recovery	Jacquarl, Mem. de la Soc. de Bolog., 1860.	Vesicles escaped in the bloody discharge.
84	22	2	1	.....	1	.....	Hemorrhage began 2d month; pain, nausea.	.....	Induced.	"	Leuers, Lancet, 1890, 954.	
85	21	0	0	.....	1	12 wks.	Vomiting severe; hemorrhage.	7 wks.	Induced.	"	Ibid.	
86	...	...	...	.....	1	.....	Hemorrhage.	.....	Spontaneous.	"	Dunn, Bost. Med. and Surg. Journ., 1885, 612.	Alarming hemorrhage.
87	35	4	...	.....	...	.....	Anasarca, anæmia, hemorrhage 3d month.	.....	.....	.....	Paddock, Phys. and Surg, 1885, 241.	Hydatids weighed; seven pounds fœtal liver attached to mole; normal child born in subsequent pregnancy.

88	...	...	...	.....	1	2 mos.	....	.....	.....	.....	Lawrence, Trans. Obst. Soc., London, 1890–91, xxxii. 65.	Uterus size of eight months at two months; enlargement due to concealed hemorrhage.
89	25	1	0	Normal.	...	19 wks.	Copious flow on 15th week; no pain.	4 wks.	Spontaneous.	Recovery	Craigin, Med. Comm., 1892, xv. 813–829.	
90	37	0	0	.....	...	4 mos.	Vomiting, slight hemorrhage.	.....	Induced.	"	Shattuck, Boston Med. Journ., 1888, 358.	
91	30	2	1	Normal.	1	.....	Vomiting and pain.	.....	Spontaneous.	"	Langevin, Journ. de Ther. Med., xxii. 248.	Mole double the size of a full-term placenta.
92	40	12	0	"	1	3 wks.	" " "	Few days.	"	"	Gilbert, Bul. de la Soc. Anat. de Paris, 1856,463.	
93	19	2	0	"	1	.....	Hemorrhage began in 5th week.	.....	"	"	Dauzats, Archiv. de Tocol., 1877, 561.	Transfused blood because of hemorrhage.
94	38	10	0	"	1	6 mos.	Nausea, vomiting, hemorrhage began 12th week; uterus grew rapidly during 4th month.	5 mos.	"	"	Budin, Ze Prog. Med., 1875, 190.	Last pregnancy ten years before the mole developed.
95	42	5	0	"	1	.....	Hemorrhage.	.....	Induced.	"	Hamon, Gaz. des Hôp., 1858, p. 283.	
96	17	0	0	.....	1	5 mos.	Pain in hypogastrium; hemorrhage.	4 mos.	Spontaneous.	"	Robin, Ibid.	
97	...	1	0	Normal.	11	5 to 7 months	.....	.....	.....	.....	Majer, Wurt. Corresp. Bl., 1843, No. 38.	All of the eleven moles were of five to seven months' development.
98	26	2	0	"	1	4 mos.	Hemorrhage at time of expulsion.	.....	Spontaneous.	.....	Magnin, Jour. de Med. et de Chir. Pract., 1881, lii. 501.	
99	21	0	0	.....	1	5 mos.	Hemorrhage sudden and profuse in 18th week.	.....	"	Recovery	Maslowsky, Centrl. f. Gyn., 1882, 144.	
100	48	6	0	Normal.	1	5 wks.	Hemorrhage.	.....	Induced.	"	Krabbel, Langenbeck's Archiv., 1878–79, 23.	Last childbirth ten years prior to mole; abdomen large as five months' pregnancy in fifth week; collapse from loss of blood.
101	48	8	...	.....	1	4 mos.	Bloody discharge for 4 months.	4 mos.	Spontaneous.	"	Jackson, Amer. Journ. Med. Sci., 1853, 375.	Last child stillborn; at time of expulsion of cysts abdomen as large as full-time pregnancy.
102	26	mult.	...	.....	1	8 wks.	Hemorrhage 8th week.	.....	Induced.	"	See Med. Brief, 1889, p. 219.	
103	26	1	...	.....	1	6 mos.	Hemorrhage late; rapid growth of uterus.	.....	Spontaneous.	"	Fruitnight, Am. Jour. Obst., 1890, 54.	
104	27	3	0	.....	1	4 mos.	Hemorrhage for 1½ mos.	2½mos.	"	"	Levers, Lancet, 1890, 954.	
105	25	5	0	Normal.	1	4½mos.	Nausea and vomiting, œdema of legs, hemorrhage for 11 weeks.	3 wks.	"	"	Oliver, Ibid., Sept. 21, 1889, 592.	
106	30	3	0	"	1	3½mos.	Slight hemorrhage.	.....	Induced.	"	Parish, Trans. Obst. Soc. Phila.	
107	27	3	0	"	1	4 mos.	Hemorrhage at 5th week.	.....	"	"	Poole, Dub. Jour. Med. Sci., 1881, lxxx. 423.	
108	26	3	0	"	1	4 mos.	Hemorrhage at 4th mo.; rapid growth of uterus.	.....	Spontaneous.	"	Ibid.	

Case No.	Age	Children.	Abortions.	Puerperium.	No.	Age.	Symptoms and course.	Duration of sympts.	Termination.	Remote results.	Reference.	Remarks.
109	...	0	0	.....	1	5½mos.	Nausea and vomiting.	.....	Induced.	Recovery	Rooker Bost. Med. and Surg. Journ., 1868, 216.	
110	35	1	0	Normal.	1	2½mos.	Hemorrhage constant.	.....	Spontaneous.	"	Routh, Lancet, 1860, 597.	
111	23	0	0	.....	1	4½mos.	Nausea and vomiting; slight hemorrhage beginning at 4th month.	2 wks.	Induced.	"	Sackett, Obstet. Gaz., Cincin., 1881–82, 174.	
112	30	6	0	Normal.	1	5½mos.	Profuse hemorrhage.	.....	Spontaneous.	"	Schultz. Zeitsch. f. Wunds. u. Geb.	
113	53	10	1	"	1	5 mos.	Nausea and vomiting, severe pain; much hemorrhage after 2d month.	.....	"	"	Schewen, Brit. Med. Journ., 1875, 101.	
114	20	0	0	.....	1	4 mos.	Nausea and vomiting, hemorrhage began at 4th month.	.....	Induced.	"	Smith, Jour. Am. Med. Assoc., 1887, 686.	
115	?	2	0	Normal.	1	3½mos.	No hemorrhage; large uterus.	.....	"	"	Ibid.	
116	13	0	0	.....	1	3 mos.	Much pain, flooding one week before birth.	.....	Spontaneous.	"	Smyth, British Med. Journ., 1873, 61.	
117	...	...	...	.....	1	.....	Jaundice.	.....	Spontaneous.	"	Thomas, Ibid., 1883, 912.	
118	30	3	0	Normal.	1	4¼mos.	Slight hemorrhage.	.....	"	"	Thompson, Proc. Conn. Med. Soc., 1880, 60.	
119	24	2	0	"	1	3 mos.	Hemorrhage began in 2d month	.....	Induced.	"	Underhill, Am. Jour. Obstet., 1879, 185.	Uterus larger than at full term.
120	25	0	0	.....	1	4 mos.	Some hemorrhage.	.....	Spontaneous.	"	Van Dyke, Med. and Surg. Rep., 1883, 10.	
121	25	20	0	.....	1	12 wks.	Hemorrhage.	10 wks.	Spontan., followed by removal with finger.	Deciduoma mal.	Fränkel, Arch. f. Gyn., 48–80.	Returned to hospital in twenty-one months; deciduoma malignum.
122	30	2	0	Normal.	1	4 mos.	Hemorrhage.	3 mos.	Induced.	"	Cazin-Segond, La Gynæcologie, 1896.	Deciduoma malignum, operated nine months after mole was expelled.
123	30	6	0	"	1	5 mos.	Hemorrhage.	.....	"	"	Müller, Verh. f. Gyn. Congress, iv. 341.	Hemorrhage great when mole was removed, and returned in a few weeks.
124	55	3	0	Normal for 10 yrs.	1	3 mos.	Continuous hemorrhage from 5th week.	Several weeks.	"	"	Mayer, Arch. f. Gyn., 1888, xxxiii. 54.	Difficult to remove adherent mole; hemorrhage profuse, and returned eleven months later.
125	..	...	...	.....	1	.....	.....	.....	.....	"	Kaltenbach, Cent. f. Gyn., 1890.	Symptoms of malignancy developed one and half years after mole was expelled.
126	24	2	0	Normal.	1	.....	Hemorrhage began in 4th month at intervals of 6 to 8 weeks.	.....	Spontaneous.	"	Nove-Josserand, Cent. f. Gyn., 1890, 265.	In 4th month uterus was size of a full-term pregnancy; hem'hage returned one month after mole was expelled.

127	47	6	1	Normal.	1	7 mos.	.....	.....	Induced.	Deciduoma mal.	Zohlein Ibid., 1890.	Malignancy devel'ed eighteen months after mole was expelled.
128	35	?	2	.....	1	6 mos.	Severe hemorrhage.	.....	"	"	Menge, Zeit. f. Geb., 1894, xxx. 323.	Severe hemorrhage return'd six months after mole was expelled.
129	18	0	0	.....	1	2 mos.	Began with profuse hemorrhage 8th week.	.....	"	"	Ibid.	Uterus was at the umbilicus in eighth week; much loss of blood when mole was removed.
130	45	8	2	.....	1	12 wks.	Continuous hemorrhage.	6 wks.	Spontaneous.	"	Bütz, Archiv. f. Gyn., 1901, xliv. 1.	One year after mole was expelled patient bled from the lungs, and died in a few days.
131	22	0	0	.....	1	8 wks.	Continuous hemorrhage.	.....	Induced.	"	Ibid.	Bilateral cysts of ovaries and interstitial endometritis.
132	36	9	6	Post-part. hemorrhage.	1	.....	Hemorrhages with liquid discharges containing cysts.	.....	Spontaneous.	Recovery	Ashley, Lancet, 1850, 319.	Frequent discharges of fluids containing cysts.
133	...	...	...	.....	...	.....	Hemorrhages.	.....	Induced.	"	Atthill, British Med. Journ., 1878, 334.	
134	42	8	3	Albuminuria.	1	.....	Hemorrhage, albuminuria.	.....	Spontaneous.	Death.	Barnes, Trans. Obst. Soc., Edinb., 1865, 117.	Cause of death uræmia; cystic ovary, uterine fibroid.
135	36	1	1	Nephritis	1	.....	.....	8 dys.	"	Recovery	Woodman, Trans. Obst. Soc., 113.	
136	24	...	...	.....	1	4 mos.	.....	10 wks.	"	Death.	Ibid.	Uterine tumor apparently seven mos. at three and a half mos.; had nephritis and anasarca and endocarditis; both ovaries cystic.
137	37	2	...	.....	1	3 mos.	Hemorrhage and anasarca.	6 wks.	"	Recovery	Bartlett, Brit. Med. and Surg. Journ., 1846, 95.	Uterine tumor at sixth week as large as at six months; threatened death from hemorrhage.
138	24	...	...	.....	1	.....	Hemorrhage and anasarca.	.....	Induced.	Death.	Bass, State Med. Assoc. of Texas, 1885, 382.	Post-partum hemorrhage cause of death.
139	49	12	...	.....	1	.....	Hemorrhage and anasarca.	0 dys.	Spontaneous.	Recovery	Brookless, Ibid., 1851, 80.	Death threatened from hemorrhage.
140	41	8	6	.....	1	4 mos.	Hemorrhage and anasarca.	2 mos.	"	"	Bethune, Canada Lancet, 1875, 161.	
141	25	0	...	.....	...	.....	.....	... ..	.....	.....	Bennett-Rich, Louisville Med. Jour., 1872, v. 337.	Dead fœtus of five months expelled with mole; lay dead in uterus three months.
142	...	...	...	.....	1	13 mos.	Hemorrhage.	7 wks.	Induced.	Recovery	Barnes, Lancet, 1886, 249	Death threatened from hemorrhage; size of uterus of seven months at three months.
143	33	8	1	.....	1	4 mos.	Hemorrhage.	.....	"	"	Phamplim, New Orl. Med. and Surg. Journ., 1885–86, 275.	
144	37	...	...	.....	1	5 mos.	Hemorrhage.	.....	Spontaneous.	"	Clark, Mich. Med. News, 1882, 89.	
145	47	12	...	.....	1	4 mos.	Hemorrhage.	.....	"	.....	Campbell, Mich. Med. Journ., 1888, 61.	

Case No.	Age	Children.	Abortions.	Puerperium.	No.	Age.	Symptoms and course.	Duration of sympts.	Termination.	Remote results.	Reference.	Remarks.
146	21	1	0	Normal.	1	4 mos.	Nausea and vomiting severe; hemorrhage began in 2d month.	2 mos.	Spontaneous.	Recovery	Depaul, Mem. de la Soc., 1850, 88.	
147	...	0	0	.....	1	14 wks.	Hemorrhage.	.....	"	"	Follin, Ibid., 1849, 67.	
148	46	4	0	Normal.	1	7 mos.	Hemorrhage.	.....	"	"	Germain, Bul. de Acad. Roy. de Med., 2d serie, 1858–59.	
149	36	3	...	"	1	8 mos.	Hemorrhage began in 6th month after quickening.	.....	"	"	Ibid.	
150	37	8	0	"	1	3 mos.	Hemorrhage began in 3d week.	7 wks.	.....	Death.	Georgic. Memosabelien, 1883, xxviii. 80.	Cause of death, hemorrhage; both ovaries were cystic.
151	28	4	0	"	1	.....	Hemorrhage continued 3 weeks.	.....	Induced.	Recovery	Ibid.	
152	49	1	0	"	1	.....	Hemorrhage.	.....	Spontaneous.	"	Garmer, Bul. de Soc. Anat., 1858, 128.	
153	37	3	...	"	1	.....	Pelvic pain, vomiting, œdema of feet; dyspnœa began 12th week; hemorrhage began suddenly in 16th week.	.....	"	"	Flamm. Rust. Mag., i.	Mole weighed six pounds.
154	37	0	0	.....	1	5 mos.	Œdema of face and feet; hemorrhage began in 2d month.	10 wks.	"	"	Dulac, Gaz. heb. de Med.et de Chir.,1884, 77.	Complicated by septic infection, anæmic convulsions.
155	34	3	1	.....	1	.....	Profuse hemorrhage in 6 to 7 months.	.....	Induced.	Recovery	.....	Vesicles expelled with blood; twin pregnancy; fœtus and placenta normal; no sign of other fœtus; mole was complete; fœtus weighed 2 lbs., and was living.
156	29	1	0	Normal.	1	6 mos.	In 3d month had vomiting, pelvic pain, palpitation; hemorrhage not spoken of.	4 mos.	Spontaneous.	.....	Melciens, Gaz. des Hôp., 1853, 482.	Mole expelled and followed by a well-formed fœtus and placenta.
157	24	0	0	.....	1	.....	Hemorrhage in 5th mo.; uncontrollable vomiting.	.....	Induced.	Recovery	Marsh, New York Med. Journ., 93.	
158	40	5	0	Normal.	1	2 mos.	Profuse hemorrhage; fever developed late in the puerperium.	.....	"	.....	Wendel, Frauenarzt, Berlin, 1887, 478.	Uterus size of five months' pregnancy.
159	26	...	...	.....	1	4 mos.	Hæmatemesis for 6 wks.; profuse flooding in 3d month.	2½mos.	"	Recovery	Croom, Edinb. Med. Jour., 1887–88, xxxiii. 297.	Blood transfused.

160	23	...	...	.....	1	6 mos.	Hemorrhage.	.....	Induced.	Recovery	Davis, Cin. Lancet, 1887, 695.	
161	21	...	...	.....	...	.....	Slight hemorrhage in 7th week, increase to flooding.	.....	"	"	Tail, Brit. Gyn. Jour., 1887, 282.	Married one month.
162	27	4	1	.....	1	9 mos.	Hemorrhage.	.....	"	"	Roeser, Gaz. de Gyn., 1885-86, 74.	Fœtal movements felt four and a half months; child developed and dead; portion of placenta normal.
163	23	1	0	Normal.	1	.....	Severe vomiting, hemorrhage profuse and sudden.	.....	Spontaneous.	"	Zwisohn, Med. Rec., 1894, 3069.	
164	28	3	0	"	1	.....	Vomiting; repeated hemorrhages, usually at night	.....	Induced.	"	Furniss, Med. Rec., 1895, 269.	One child and two abortions have since followed.
165	32	5	0	"	1	4½mos.	No bloody discharge.	.....	Spontaneous.	"	Ibid.	
166	32	4	0	"	1	4 mos.	Nausea, vomiting.	.....	Induced.	"	Ibid.	Twins and two other children since; collapse.
167	24	0	0	.....	1	4 mos.	Nausea, vomiting, albuminuria; no hemorrhage.	.....	"	Death.	Ibid.	Meningitis; no autopsy.
168	22	0	0	.....	1	3 mos.	Nausea, vomiting.	.....	Spontaneous.	Recovery	Ibid.	
169	23	0	0	.....	1	3½mos	Uncontrollable vomiting, bloody discharge	.....	"	"	Ibid.	Collapse from hemorrhage.
170	40	13	1	Normal.	1	4½mos.	Slight pain, no hemorrhage; no unusual distention of uterus.	.....	Induced.	"	Cremen, Dub. Journ. Med. Sci., 1858, xxv. 473.	
171	28	1	...	"	1	7½mos.	Slight pain, hemorrhage commenced 4th month; some over-distention of uterus.	3½mos.	Spontaneous.	"	Crossman, Brit. Med. Journ., 1867, 24.	
172	17	0	0	.....	1	8 mos.	Hemorrhage 7½ months.	2 wks.	Induced.	"	Edis, Ibid., 1871, 353.	
173	42	7	1	Normal.	1	4½mos.	Uncontrollable vomiting, pain, hemorrhage at 3d month; great distention.	6 wks.	Spontaneous.	"	Edwards, Lancet, 1847, vol. i.	
174	32	?	...	.....	1	.....	Slight hemorrhage.	.....	Induced.	"	Hehle, Wien. med. Presse, 1871.	
175	36	7	0	.....	1	3 mos.	Slight hemorrhage.	.....	"	"	Koch, Zeit. f. W. Mds. u. Geb.	
176	40	?	...	.....	1	3½mos.	Nausea and vomiting; hemorrhage.	.....	Spontaneous.	"	MacGill, Amer. Jour. Med. Sci., 1827, 240.	
177	25	1	0	.....	1	4½mos.	Nausea, vomiting, hemorrhage at 3½ months.	4 wks.	"	"	Mellor, British Med. Journ., 1865, 282.	

Case No.	Age	Children.	Abortions.	Puerperium.	No.	Age.	Symptoms and course.	Duration of sympts.	Termination.	Remote results.	Reference.	Remarks.
178	17	0	0	.....	1	4 mos.	Constant nausea and vomiting, œdema of feet; hemorrhage at 6th month.	10 wks.	Induced.	Recovery	Miller, Trans. Med. Sci., W. Va., 1879, 488.	
179	50	7	3	.....	1	2½mos.	Nausea and vomiting; hemorrhage at 6th wk.	6 wks.	Spontaneous.	"	Moorehead, Lancet, 1863, 305.	Sterile for past twenty years before mole.
180	50	10	0	.....	1	3⅓mos.	Bloody discharge constant, beginning 6th wk.	8 wks.	"	"	Moore, Dublin Quart. Med. Sci., 1868, 473.	Sterile for ten years before mole.
181	...	3	0	.....	1	6 mos.	Pain severe, hemorrhage at 4th month.	2 mos.	"	"	Morris, Boston Med. Journ., 1845, 1, 17.	
182	32	6	...	.....	1	8½mos.	Pain in chest.	.....	"	"	Ibid.	Weight of mole six pounds.
183	...	...	...	.....	1	6 mos.	Uterus larger than at term.	.....	Induced.	"	Moses, St. Louis Cour., 1879, 104.	
184	19	0	...	.....	1	3 mos.	Nausea and vomiting; slight hemorrhage after 2d month.	1 mo.	"	"	Mundell, Journ. Amer. Med. Assoc., 1888, 592.	
185	29	...	...	.....	1	6 mos.	Constant nausea and vomiting; œdema of feet; hemorrhage severe 2d month; great distention.	4 mos.	Spontaneous.	"	Murphy, Obst. Gaz., Cincinnati, 1880, 111.	
186	25	5	...	Normal.	1	4½mos.	Slight bleeding 9th wk.; later abdominal pain.	9 wks.	Induced.	"	Gerson, Univ. Med. Mag., Philadelphia.	Extreme anæmia.
187	...	...	...	.....	1	11 wks.	Excessive vomiting, hemorrhage in 9th wk.	.....	"	"	Kempf, Ind. Med. Journ., 1898, 53.	
188	26	9	0	"	1	8 mos.	Had flooded 7 times.	.....	"	"	Nariman, Ibid., 1898, 853.	
189	24	2	0	"	1	.....	Uncontrollable vomiting 9th month; continuous hemorrhage.	.....	"	"	Kennedy, Univ. Med. Mag., 1893-94, 677.	
190	52	8	0	"	1	.....	Hemorrhage; no pain.	4 wks.	Spontaneous.	"	Heagey, Med. News, 1894, 381.	
191	18	1	0	"	1	11 wks.	Hemorrhage 6th week.	4 wks.	"	"	Gillette, Med. Rec., 1896, 15.	
192	40	mult.	0	....	1	10 wks.	Hemorrhage 6th week; pain in 8th week	4 wks.	"	"	Champneys, The Practitioner, 1896, 15.	Sepsis followed; curetted three times.
193	33	0	0	.....	1	.....	Hemorrhage and pain late.	.....	"	Death.	Ibid.	Cause of death peritonitis.
194	18	1	0	Normal.	1	.....	Severe pain in pelvis in 6th month; no loss of blood until this time.	2 wks.	Induced.	"	Ibid.	Thought to be a soft fibroid; two mos. after mole was expelled septic symptoms developed. Patient died, probably from syncytioma malignum and septic peritonitis.
195	25	0	0	.....	1	.....	Severe hemorrhage in 5th week.	.....	Spontaneous.	Recovery	Dirmoser, Wien. Med. Woch., 1896, 432.	

196	23	0	0	.....	1	5 mos.	Hemorrhage.	.....	Spontaneous.	Recovery	Hastings, Canada Practitioner, 1896, 203.	
197	22	0	0	.....	1	.....	.....	.....	"	"	Cronkite, Med. Rec., 1897, 239.	
198	22	2	0	Normal.	1	.....	Quickening felt; hemorrhage at 7th mo., slight; great abd. enlargement.	3 mos.	"	"	Anderson, W. Lond. Med. Repository, 1827, xxviii, 40.	Mole weighed five pounds.
199	16	0	0	.....	1	6 mos.	Weak, anæmic, pain, no hemorrhage; rapid growth of uterus.	.....	"	"	Jno. Andrew, Glasgow Med. Journ. 1832, lxviii. 74.	
200	...	1	1	Normal.	1	4 mos.	Nausea, slight spitting of blood; no hem'rhage; uterus size of 6 months' pregnancy.	.....	"	"	Ibid.	Mole weighed seven pounds.
201	...	0	0	.....	1	4 mos.	Nausea; no hemorrhage; spitting of blood; abnormally large uterus.	.....	Spontaneous and induced.	"	Ibid.	
202	...	1	0	Normal.	1	.....	Rapid growth of uterus.	.....	Induced.	Death.	Armstrong, Liverpool and Manchester Med. & Surg. Rep., 1874, 53.	Death from hemorrhage at time of delivery.
203	30	...	...	.....	1	term.	Hemorrhage slight from 5th month.	4 mos.	"	Recovery	Bernardy, not report'd	Profuse hemorrhage in labor.
204	36	7	0	Normal.	1	10 wks.	Hemorrhage at 8th wk.; moderate distention.	2 wks.	"	"	Borden, Med. News, 1884, xlv. 703.	Only four cysts in placenta; no fœtus.
205	38	4	1	"	...	4½mos.	Constant vomiting; emaciation, hemorrhage beginning 2d month.	10 wks.	"	"	Bryan, British Med. Journ., 1872, 464.	
206	...	0	0	.....	1	5 mos.	.....	.....	Spontaneous.	"	Chrone, Lancet, Nov. 11, 1843.	
207	35	9	0	Normal.	1	2½mos.	Vomiting, ankles swollen, no hemorrhage.	.....	"	Death.	Chunn, Maryland Med. Journ., 1882, 550.	Heart lesion. Died of post-partum hemorrhage; size of six months pregnancy at two and a half months.
208	25	0	1	.....	1	4 mos.	Extreme anæmia; rapid growth of uterus.	10 wks.	"	Recovery	Findley, not reported.	Healthy child born since mole, and patient again pregnant.
209	36	5	0	Normal.	2	15 wks.	Extreme anæmia, continuous hemorrhage; rapid growth of uterus; rigor, slight temperature	.....	Hysterectomy.	"	Ibid.	Both ovaries cystic, patient now in good health.
210	...	...	...	.....	1	8 wks.	Pain in pelvis 5th week; hemorrhage severe in last few days.	3 wks.	Induced.	Deciduoma mal.	Bonnaire & Tetuille, Rev. de Gyn. et de Chir., 1901, No. 4.	Death five weeks after mole was removed; hysterectomy performed.

6. The length of time a mole remains *in utero* does not influence its disposition to become malignant. Those expelled in the early months are as likely to become malignant as those of late development.

7. The diagnosis cannot be made with certainty without seeing the vesicles. These vesicles are seldom expelled spontaneously before the abortion is in progress (4 times in 210 cases); hence it is that the diagnosis is rarely established until the expulsion of the mole, either spontaneous or induced.

8. The most constant clinical evidence of the presence of a mole is the rapid development of the uterus. Uterine hemorrhage is an early and almost constant symptom. The irregular shape and consistency of the uterus are important diagnostic factors.

9. In view of the tendency of hydatiform mole to undergo malignant degeneration, our only safeguard lies in early recognition and immediate removal, however limited the degeneration may be.

10. Ergot and vaginal packs will control the hemorrhage, and will often excite the uterus to contract and expel the mole. The curette should not be used, for fear of perforating the greatly stretched and weakened walls.

11. After the mole is expelled always explore the uterus with the finger, irrigate, and pack with antiseptic gauze.

12. Two weeks after the birth of the mole it is well to curette the uterus and examine the scrapings for syncytial invasion, and, if found in the act of proliferating, hysterectomy should be performed.

13. A period of about three years of watchful expectancy should follow the expulsion of a hydatiform mole. In the event of uterine hemorrhage an exploratory curettage must be made for microscopic examination of the scrapings. All new-growths in the vagina and lungs are to be regarded with suspicion.

14. The tables are a summary of statistics derived from the accompanying reports of 210 cases: Average age of patient is twenty-seven years; extreme ages are thirteen and fifty-eight years. Largest number of moles born of a single woman is eleven. Eight of the 210 cases had cystic degeneration of the ovaries. One hydatiform mole developed in the Fallopian tube. Malignant degeneration occurs from one week to four and one-half years after the expulsion of the mole, as evidenced by the recurrence of hemorrhage. Maternal mortality in hydatiform mole is 25 per cent. Causes of death: Syncytioma malignum, 16 per cent.; hemorrhage, 4 per cent.; septic peritonitis, 2 per cent.; general sepsis, uræmia, nephritis, endocarditis, meningitis, each 0.005 per cent.; two of unknown cause.

15. Contrary to the usual statement that there is a tendency to the development of two or more hydatiform moles, it is found to be the great exception.

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For further references see accompanying tables of reported cases.

ENTRANCE OF AIR INTO THE VEINS.

A REPLY TO DR. HARE.

By Malcolm Goodridge, M.D.,
of New York City.

In an article on this subject in the November number of The American Journal of the Medical Sciences, Dr. H. A. Hare, of Philadelphia, takes issue with me on several points brought out in my paper, which was published in the September issue of this Journal. As some of his criticisms, if left unchallenged, would destroy the value of my work as a careful research, I shall take this opportunity of defending various statements made in my original paper.

In the first place, let me rehearse the points which we intended should be brought out in that article. They are briefly as follows:

1. That there were a sufficient number of well-authenticated cases on record of deaths due to air embolism to warrant the dread that existed of this accident.

2. That a considerable difference of opinion existed between Hare on the one hand and Senn on the other, as to the amount of air it was necessary to inject into the veins to produce death; and that in the main my views were in sympathy with those of Senn on this subject.

3. That the statement made by Dr. Hare in his conclusions, that "death never occurs from entrance of air into the ordinary veins of the body unless the quantity be enormous—from one to several pints"[1] —was not corroborated by the results obtained in my experiments.

4. That death was due to gaseous distention of the right heart or to air embolism of the coronary vessels.

5. That in the treatment of this condition, should the accident occur in the human subject, combined aspiration of the right ventricle and venous infusion with warm salt solution was more efficacious than either of these methods singly.

Dr. Hare, in the beginning of his review of my paper, questions the correctness of the following statement: "Senn found that small quantities of air when injected into the veins proved fatal in a large percentage of his dogs." My use of the word "small" in this sense was purely comparative, and referred to my statement that in such experimentation the "personal equation played no insignificant part," in view of the vastly different results obtained by Dr. Hare and Dr. Senn in their respective experiments.

I know of no better way of proving the correctness of my statements on this point than by quoting directly from the original papers of Hare and Senn. Hare says in the early part of his paper that "the object of this paper is to prove by actual experiment that the air on entering the veins is not capable of deleterious influences;"[2] and Dr. Hare experimented on some seventy-five dogs, injecting air in quantities varying from a few bubbles to 40 c.c., and never had any ill results, save for a slight transitory fall in blood pressure. Senn, on the other hand, early in his article says: "I intend on this occasion to call your attention to one of the most dreaded and, I may add, one of the most uncontrollable causes of sudden death. I refer to air embolism."[3] In the course of his experiments Senn injected a dog weighing sixty-five pounds with 30 c.c. of air, the result being that "the heart's action became very tumultuous and intermittent; respirations were rapid and superficial;" . . . "the dog appeared unwell for several days."[4] . . . This surely does not coincide with the results obtained by Dr. Hare in his experiments.

Senn after injecting some ten animals, one of which was a sheep, with air—the maximum amounts used being 150 c.c. in the case of the sheep, which weighed ninety-five pounds, and 90 c.c. in a seventy-five-pound dog—says: "With the exception of Experiment 8 it may be safely assumed that all the animals would have died had aspiration not been performed."[5]

In Experiment 3 of this group of Dr. Senn's animals a dog weighing forty pounds was injected with 45 c.c. of air, and "the symptoms became so grave that death seemed unavoidable."[6] Aspiration of the right ventricle was performed, and the dog recovered.

Dr. Hare, at the close of his original paper, says: "Death never occurs from the entrance of air into the ordinary veins of the body unless the quantity be enormous—from one to several pints;"[7] while Dr. Senn states that "dogs weighing about thirty pounds would usually recover in a short time after an injection of 30 c.c. of air, double that amount constituting generally a fatal dose."[8]

I have entered into this somewhat detailed comparison of the sayings of Senn and Hare in order that I might show that a decided difference of opinion on this subject existed among medical men, and that it was precisely this disparity that led me to believe that the "personal equation played an important part," though the results obtained in my own experiments coincided with those obtained by Dr. Senn.

Dr. Hare quotes from my paper as follows: "The entrance of air into the veins even in small amounts is to be dreaded, as it results in death," and doubts whether this conclusion is justified by my own experiments. Dr. Hare has inadvertently misquoted me. The correct quotation should have read: "The entrance of air into the veins is to be dreaded, as it *may* result in death." The omission of the word "may" in Hare's version of my statement quite changes the meaning of the whole sentence, making it much more radical than was intended. In several places in my article I distinctly state that a certain small percentage of my dogs did require large quantities of air to be injected into the jugular vein before death occurred. My conclusion was based on the possibility of a fatal termination after comparatively small venous injections; and my claim was that Senn's original experiments, and later my own, gave ample justification for this opinion, and for the same reason there seemed to be good ground for disputing Dr. Hare's radical statement that "death never occurs from the entrance of air into the ordinary veins of the body unless the quantity be enormous—from one to several pints."

Dr. Hare's next criticism of my paper is based on his opinion that I erred seriously in the amount of air injected. In most of my animals this amount was 75 c.c. This quantity was not chosen arbitrarily, but

was founded on the statement made by Dr. Senn that 60 c.c. were usually a fatal dose in dogs weighing thirty pounds. As nearly all my dogs were from four to twenty pounds heavier than this, a proportionately larger amount of air was selected for the injections.

Dr. Hare goes on to say: "While if any further proof of the fact that air may enter a vein without producing death is needed, I may state that I have in my own experience seen a considerable quantity of air—amounting to as much as from 2 to 3 c.c.—injected into the median basilic vein of two human beings without producing any symptoms whatever."

I have never denied, as I have before stated (*vide supra*), that air *may* enter a vein without producing death. Dr. Hare's hypothesis is wrong, and he criticises a statement that was never made by me. I am at a loss to understand, however, if Dr. Hare considers 2 to 3 c.c. a considerable quantity of air, what, in his opinion, would constitute a small quantity, based on these figures.

Dr. Hare next refers to one of my published experiments (No. 10) as an example of the fact that recovery may take place after an injection of 75 c.c. of air into the jugular vein, but takes no notice of the fact that this dog was treated by aspiration of the right ventricle and warm saline infusion, and that in my opinion it was due to this treatment that recovery took place. This same dog, five days later, was injected with precisely the same amount of air. No treatment was resorted to, and the dog died. After waiting for five minutes, the animal during this time showing no signs of life, autopsy was performed, with the following result: "The auricles were spasmodically contracting, the right ventricle was distended with air, the heart was fibrillating, and *the coronary vessels were filled with air emboli.*" I have emphasized this last sentence for two reasons:

The first is that I regard it as the most important condition revealed by the autopsy, as it was upon this phenomenon, found in nearly all the animals which came to autopsy, that I based my opinion that coronary embolism was one of the chief causes of death following entrance of air into the veins.

My second reason for laying particular stress upon this point is that Dr. Hare omits it entirely when quoting from the results of my autopsy. Dr. Hare believes that had autopsy been postponed "the dog might have survived even the second injection." A heart which is fibrillating may, of course, be made to contract co-ordinately again; but when it is thrown into fibrillation as a result of some mechanical interference with the intrinsic circulation of the heart I do not believe that co-ordinate contractions can be continuously maintained until that obstruction is removed.

In referring to my Experiments Nos. 13 and 15, Dr. Hare dwells on

the point that it was necessary in these two instances to inject enormous quantities of air before death resulted. This I will not dispute; in fact, I frankly admitted in my article that these two animals did require large quantities of air to be injected into their jugular veins before the pulse tracings on the kymograph entirely disappeared.

At the close of his review of my paper Dr. Hare voices the opinion that "in all probability different resistance to air embolism exists in different animals." "Rabbits and monkeys are very susceptible, whereas dogs and goats are extraordinarily immune." If this be true —and I believe that it is—then I object to Dr. Hare's applying the results of experiments on dogs to man, weight for weight, as he does when he says, in referring to Experiment 15, "it required 400 c.c. to produce death." "The equivalent to this injection in a man of 160 pounds would be three pints of air." It is improbable that precisely the same degree of immunity exists in both dog and man, and we have every reason to believe that man is extremely susceptible.

In conclusion, I wish to reiterate that not only have I never denied that some dogs may require large quantities of air to be injected into the jugular vein before death results, but I have actually shown this to be a fact in certain of my experiments. In all of the dogs used in our experiments, when 75 c.c. of air were injected into the jugular vein the following symptoms developed: There was a sudden fall in blood pressure; a churning sound was heard over the precordia; the heart at first was tumultuous, and was later rapid, weak, and irregular, and the respirations were gasping. While a small percentage of these dogs eventually recovered without treatment, I think should this series of symptoms occur on the operating table in the human subject, it would be justly considered an "unfavorable result."[10]

In light of the testimony of reputable surgeons, based on clinical experience, Senn's experiments, and the results obtained in my own work in this line, I still believe with Dr. Kemp when he says: "Statements that the entrance of small quantities of air (into the veins) need not be a source of anxiety we believe to be pernicious teaching and to lead to carelessness."[9]

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REVIEWS.

A Treatise on Diseases of the Eye, Ear, Nose, and Throat. By various authors. Edited by William Campbell Posey, A.B., M.D., and Jonathan Wright, M.D. 1238 pages, 650 engravings, and 36 colored plates. Philadelphia and New York: Lea Brothers & Co., 1903.

This is pre-eminently a work for the general practitioner and the beginner in these allied specialties. Considering that the book is written by several authors, it is welded into a complete whole in an astonishing way. Directness of treatment is the note sounded by the ophthalmic editor in the opening chapter, which is a clear, comprehensive setting forth of what is essential in the systematic examination of the eye. Duane's observations on Refractive Errors in General is one of the strongest things he has written, and, along with Wood's splendid chapter on Motions of the Eyeballs and Their Derangements, comprises some of the soundest information and advice to students as to refraction and muscular anomalies we have seen. The chapter on the Conjunctiva, Cornea, and Sclera, by Weeks, is exactly what would be expected from this distinguished author. The division of the various phases of conjunctivitis into those of specifically known etiology and those not yet so identified is wise. The old-time clinical classification is doomed, and it is gratifying to note how many of the inflammations of the conjunctiva are placed in the etiologically known column by Weeks. The chapter on the Embryology of the Eye and Diseases of the Iris, Ciliary Body, Choroid, and Vitreous is somewhat condensed, but so profusely and beautifully illustrated as to more than make up for any lack of text. Moreover, Würdemann's careful and yet easy style makes of this an unusually valuable chapter. Gifford's chapter on "Sympathetic Ophthalmia and Foreign Bodies in the Eye" is the *piece de resistance* in the ophthalmic portion of the volume. The author's supreme mastery of his subject is everywhere evident. There is nothing quite like it in our language, and we commend it to the earnest study of ophthalmologists and general practitioners alike. Diseases of the Retina, Optic Nerve, and Optic Tract have been safely intrusted to Spicer, whose wide clinical experience with these diseases is so well known. The editor is to be especially congratulated on having secured Treacher Collins to write the chapter on Glaucoma. His ideas as to the etiology of glaucoma are based upon pathological findings rather than speculation, and are deserving of the fullest consideration. His closing remarks on the clinical application of treatment in glaucoma embrace all that is really worth while in the management of this dread malady. The Eye as Related to General Disease is most exhaustively gone into by Clark, who has contributed a chapter for which both the ophthalmic and general worker will be grateful. The intimacy of this relation becomes daily more apparent and important both to diagnosis and treatment. For the introduction of this chapter, which, we believe, is the first time any of its kind has appeared in an English or an American text-book on

ophthalmology, the editor deserves much praise. The contributions of Reeve, Suter, Ellett, Starr, Veasey, and Shumway all lend strength to the work.

Under the able editorship of Dr. Jonathan Wright the portion of the book dealing with diseases of the nose, throat, and ear are written in accord with the high standard maintained by the section devoted to diseases of the eye. Dr. Goodale's chapter on the histological pathology of diseases of the nose and throat is a notable exposition of the proper methods to be pursued in this line of work. The various methods of examination of the nose and throat are clearly explained by Newcomb. The chapters by Richardson, Simpson, and Casselberry on Diseased Conditions of the Nose and Throat and Their Treatment, and that by St. Clair Thomson on the Accessory Sinuses are each of them excellent. Dr. Birkett's chapter on Diseases of the Oro- and Nasopharynx is especially notable for the excellent illustrations which accompany it. It is to be regretted that Dr. Hopkins, in his otherwise excellent chapter on Deformities of the Nose, makes no mention of the use of paraffin by subcutaneous injection. For special commendation in the section on Diseases of the Ear we would mention Alderton's chapter on Purulent Inflammation. It is excellent in every particular.

If there must be criticism, it would be that the book is bulky. However, it is well made and lavishly illustrated. Altogether it is a splendid addition to our literature, and ought to prove a very present help in time of trouble to those who count their books as friends.

W. R.

Diseases of the Eye. A Handbook of Ophthalmic Practice for Students and Practitioners. By G. E. de Schweinitz, A.M., M.D., Professor of Ophthalmology in the University of Pennsylvania, Consulting Ophthalmic Surgeon to the Philadelphia Polyclinic, Ophthalmic Surgeon to the Philadelphia Hospital, Ophthalmologist to the Orthopædic Hospital and Infirmary for Nervous Diseases. With 280 illustrations and 6 chromo-lithographic plates. Fourth edition, thoroughly revised. Philadelphia and London: W. B. Saunders & Co., 1903.

The first edition of this work appeared in 1892. Four editions besides the supplementary one of the first have been required since that time. This shows clearly what a place this fine book has made for itself. This edition contains about 150 pages more than the first.

The first four chapters deal with optical principles, ophthalmoscopy, ophthalmometry, refraction of the eye, functional testing, and examination. These chapters are clear and full, embracing more than a quarter of the entire work—not too much, as this department of ophthalmology is largely *sui generis* and the most specialized of the whole, presenting the greatest difficulties to the student. The author does not offer a simple epitome of the principles intelligible only to the reader who is already acquainted therewith, but has succeeded in putting them in such a form as to meet the requirements of the novice as well. These chapters have been largely rewritten for this edition.

Among the many interesting points brought out we select a few: Tscherning's view of the accommodation—that it does not depend on relaxation of the zonula, but on its tension, flattening the peripheral

portion of the lens and increasing the curvature of the centre—is given, as well as the older view of Helmholtz.

The normal temperature of the lower fold of the conjunctival sac is stated to be 96° F. There is an average increase of 1.7 F. in inflamed eyes. The highest is found in acute iritis.

Jackson's binocular magnifying lens is commended. We fail to find any reference to Thorner's beautiful ophthalmoscope.

Homatropine, if properly used, is indorsed as giving "very satisfactory results" as a cycloplegic. Atropine, hyoscyamine, hyoscine, duboisine, and scopolamine are also mentioned as efficient cycloplegics. Euphthalmine and cocaine are active mydriatics, not cycloplegics. Ephedrin homatropine 1-10, mydrol 10 per cent., and atrocin are referred to.

In ordering glasses for hypermetropia allowance for range is properly insisted upon. Why does not the same apply to myopia?

In myopia full correction is the object to be attained in young persons, no matter how high the myopia, if the vision is full and binocular vision exists. When the visual acuity is imperfect or binocular vision lost, it is better to order partial correction for near work. Of removal of the clear lens in high myopia, the author states that his experience, though limited, has been favorable.

Among the eighteen varieties of keratitis described special paragraphs are devoted for the first time in this edition to relapsing traumatic bullous keratitis, keratitis *annularis et disciformis*, grill-like keratitis, atheromatous ulcers of the cornea, or scar keratitis. The latter attacks corneal scars and staphylomas, leading in some cases to purulent ulcers.

Sympathetic inflammation is sharply differentiated from sympathetic irritation. In the treatment, intraocular as well as subconjunctival injections of bichloride of mercury are condemned. Alberti's statistics are quoted in support of the view that sympathetic ophthalmitis is not as grave as formerly. Mr. George Critchett's operation is recommended for the complicated cataract formed by the union of iris, lens, and capsule in some cases.

Of the symptoms of heterophoria the author remarks that "many instances of remarkable nervous disturbances are associated with heterophoria, especially hyperphoria (as well as with refractive errors), and cure will often follow the relief of the ocular difficulty. Unfortunately, the whole matter has not always escaped exaggeration." The author does not appear to think very highly of operative interference in these cases. While he admits that "brilliant results have been made and described, a good deal of injudicious snipping of the tendons of the ocular muscles has been practised."

A special feature of the book is the place given to the newer remedies. Holocaine is praised as an "admirable local anæsthetic." It does not affect the pupil, nor the accommodation, nor increase the intraocular tension. Dionin is mentioned as a remedy in corneal ulcerations, inflammations of the uveal tract, and glaucoma. The author's experience with it has been unsatisfactory. Acoin finds no favor.

An appendix deals with the ophthalmometer and Stevens' strange instrument, "the tropometer." Description of the latter might perhaps have been omitted without depriving the reader of much useful information.

The excellence of this work, however, cannot be justly estimated from isolated extracts. As a whole, it is an adequate and satisfac-

tory exposition of the subject with which it deals. Sanity of view characterizes it throughout. There is absolutely no riding of hobbies. Finally, we cannot lay down the book without expressing our admiration for its excellent English, making a perusal of the work a source of pleasure as well as of instruction. T. B. S.

DILATATION OF THE STOMACH. By M. SOUPAULT, Médecin de hôpitaux de Paris. One volume, 96 pages, with figures in the text. Pasteboard (Actualitiés médicales). Paris: J. B. Baillère & Sons, 1902.

The author presents the question of the dilatation of the stomach in a clear and precise manner. A careful clinical analysis, aided by the most precise technical procedures, has shown that the increase in the capacity of the stomach and the motor insufficiency which accompanies it are in reality a secondary state, the pathological significance of which is directly dependent upon the most variable causes. The author first studies the symptoms common to all dilatations, then their etiology and pathology, developing in detail the question of dilatations of pyloric origin, dilatations from extrinsic causes, and dilatations from an insufficient motor action of the walls.

Practically half of the book is devoted to the treatment of the affection. First, the general hygienic measures are discussed which are necessary to the general treatment of all varieties of dilatation; then the more special treatment of the dilatation of pyloric origin and of insufficiency are given in detail. W. T. L.

A HANDBOOK OF MATERIA MEDICA, PHARMACY, AND THERAPEUTICS. By SAMUEL O. L. POTTER, A.M., M.D., M.R.C.P., London, formerly Professor of the Principles and Practice of Medicine in the Cooper Medical College of San Francisco; Major and Surgeon of Volunteers, U. S. Army, etc. Ninth edition, revised and enlarged. Pp. xiii., 951. Philadelphia: P. Blakiston's Son & Co., 1902.

THIS edition, in addition to the matter contained in its predecessor, embodies the three years' experience of the author in a tropical climate in both civil and military practice. In the materia medica portion forty-three articles are either new or rewritten; some of the new ones, however, are not extensive—*e. g.*, that on euquinine, which appears as equinine in the preface. In the therapeutic section forty-five articles are added or presented in a new dress. This does not fully record the changes, for in a large number of instances condensations, elaborations, or substitutions are met with. The book is enlarged but little as compared with the extent of revision. The work has always appealed to us as an excellent one for the physician who may use it for study or reference; of less value, perhaps, to the student who likes to learn his bearings and the relationship of remedies. Its dictionary-like arrangement gives valuable but disconnected information. For the physician, as a practical work by one whose labors have been performed under various

conditions and who has undergone varied experiences, therapeutic as well as medical, this edition represents experience and erudition. In particular this volume has much of the hereditary character of the earlier editions, and in places we find the author relying upon himself to a greater degree and ignoring the classical treatment of various symptoms and diseases. To the alert practitioner the personality of this part of the book appeals strongly, although its author be at the antipodes. If the general trend is optimistic it is because the physician should carry cheer to the patient and not the despair of the dead-house. Yet it is safely optimistic, not relying upon conclusions based on scanty data. For the author's success in intelligently, conscientiously, and acceptably presenting his subject, or rather group of subjects, the demand for large editions so frequently shown is proof; and to the testimony to the author's learning and labors, we here, as we have in other places, desire to add our own. R. W. W.

THE DISEASES OF INFANCY AND CHILDHOOD. Designed for the Use of Students and Practitioners of Medicine. By HENRY KOPLIK, M.D., Attending Physician to the Mount Sinai Hospital; ex-President of the American Pediatric Society, etc. Illustrated with 169 engravings and 30 plates in color and monochrome. New York and Philadelphia: Lea Brothers & Co., 1902.

IN the space of 650 pages Dr. Koplik has succeeded in making a very satisfactory presentation of pediatric knowledge of the present day, and as far as we can observe, after a careful examination of his work, has omitted nothing of importance that properly belongs within the scope of his subject. From the moderate size of the volume it is evident that a special effort has been made to avoid discursiveness and unnecessary verbiage. The style is incisive, the sentences short and direct—a characteristic which is noticeable throughout the volume, but most markedly so in the earlier pages, in which at times this effort at brevity is rather too apparent. On cursory examination the first thought that strikes the reviewer is the admirable discretion exercised in the choice and presentation of illustrations. In this era of the handy camera there is always a great temptation to make a picture-book of a purely medical work, more often, perhaps, at the solicitation of the publishers than in accordance with the better judgment of the author. Dr. Koplik's illustrations, however, are always well-chosen and illuminating, especially the plates reproduced from the pen-and-ink and wash drawings of Dupuy. As a rule, these are much better illustrations of morbid conditions than the usual half-tones from direct photographs, which often fail to emphasize sufficiently the salient features of disease.

The usual classical arrangement of the subject-matter is followed out, though special commendation may be given to the introductory sections which open the various chapters. These deal with general symptomatology and special methods of examination. Thus, the chapter on nervous diseases begins with a consideration of the normal cerebro-spinal fluid and the changes to be expected in various morbid conditions of

the cerebro-spinal system. This is followed by a concise description of the operation of lumbar puncture and the indications for its employment.

The consideration of methods of infant feeding is somewhat disappointing. Dr. Koplik does not believe in formulæ for milk modification, with which, he admits, he has not had an extensive experience, but he speaks vaguely of calculating the proportions required in an "easily remembered method of home modification" in these words: "The other method of which I have made use requires cream containing 16 per cent. of fat. With ordinary milk and a 6 per cent. solution of sugar of milk, assuming the composition of cow's milk as above [proteids, 3.5 per cent.; fats, 3.6 to 4 per cent.; and sugar, 4 per cent.], we first calculate the proteid composition of the mixture, diluting with the 6 per cent. sugar of milk solution. This gives us, if we dilute the milk, a mixture having the absolute proteids and a certain percentage of fat and sugar. The sugar is ignored. We then add to this the requisite amount of the 16 per cent. cream to bring the fats up to the required strength, allowing for the fat already in the dilution. This is simply a matter of calculation, and can be worked out by anyone if the required materials are at hand." To the inquiring student who wishes to know how Dr. Koplik does this, the description of his method just quoted will prove an interesting *lucus a non lucendo*.

Aside from this criticism, which is so obviously invited, little but praise can be given to the general presentation of the subject-matter. Dr. Koplik writes with conviction and with an authoritative grasp of his subject, while a judicious conservatism characterizes his diagnostic and therapeutic methods. The bacteriology is full and up to the hour, being especially well treated in the consideration of the pulmonary and cerebro-spinal infections. For a general text-book, the chapter on diseases of the heart and pericardium is one of the most satisfactory presentations of the subject we are familiar with.

For a first edition very few typographical errors are to be found. One very curious one is the repeated mis-spelling of the name of Dr. Maynard Ladd, of Boston, as Lladd. The type is large, and the book is beautifully printed on heavily calendered paper—a fine specimen of modern book-making. An index of authors precedes the general index, which is quite full and satisfactory, and at the end of each chapter is given a list of the leading authorities quoted, with the references. The book is a distinctly valuable addition to our list of pediatric text-books.

T. S. W.

BIOLOGICAL LABORATORY METHODS. By P. H. MELL, Ph.D. New York: The MacMillan Company, 1902.

THE author states in his introduction that it has been his endeavor to begin at the beginning and to treat his subject in a scientific, accurate manner, yet at the same time as clearly and as simply as possible, and we think he has thoroughly fulfilled his purpose.

The book forms a very complete exposition of the most advanced methods used in laboratory work, and will be found of value not only as a text-book by teachers of the subject, but by the large class of students who are self-taught or desire a laboratory companion as a guide to the most recent methods of work.

J. H. G.

THE PUBLIC AND THE DOCTOR. By a REGULAR PHYSICIAN. Published by Dr. B. E. HADRA, Dallas, Texas.

THIS little book, if utilized in the manner intended by its author, should prove of very considerable utility not only to physicians but to their patients. It explains in untechnical language the various interrelationships arising between doctors and their patients. It tells why physicians "disagree;" gives timely warning against the pseudophysicians who thrive like locusts on the American public, and deals with all of those many vexatious little questions which arise to puzzle the layman's mind concerning what he has a vague dread of under the term "medical ethics." Its author suggests that it would be well for physicians to present copies of his work to their patients, and we heartily indorse his suggestion. R. M. G.

A REFERENCE HANDBOOK OF THE MEDICAL SCIENCES, EMBRACING THE ENTIRE RANGE OF SCIENTIFIC AND PRACTICAL MEDICINE AND ALLIED SCIENCE. By various writers. A new edition, completely revised and rewritten. Edited by ALBERT H. BUCK, M.D., New York City. Vol. V. New York: William Wood & Company, 1902.

THIS volume presents a series of articles of particular value to the general practitioner as well as a number of articles which will appeal chiefly to the specialist. Of the latter we would mention particularly the articles upon the larynx and its diseases and those which deal with insanity and idiocy. They form very complete expositions in both instances of the most recent scientific progress in the subjects whereof they treat. The anatomy and pathology of the kidneys and the diseases of those organs are treated with great exhaustiveness. One of the most interesting topics which will be found completely covered in this volume by a number of different articles is the relation of insects to disease. It is hard for a physician to get at the literature and most advanced views on a subject such as this, and it is, therefore, particularly valuable for him to have the matter rendered available in the excellent way in which it is in the *Handbook*. The volume is, as are all of the set, profusely illustrated. F. R. P.

THE PRACTICAL MEDICINE SERIES OF YEAR BOOKS, COMPRISING TEN VOLUMES ON THE YEAR'S PROGRESS IN MEDICINE AND SURGERY. Issued monthly under the general editorial charge of GUSTAVUS P. HEAD, M.D. Vol. I., General Medicine. Edited by FRANK BILLINGS, M.S., M.D., and J. H. SALISBURY, M.D. October, 1902. Chicago: The Year Book Publishers.

VOLUME I. of this series amply maintains the high standard of those which have preceded it. The abstracts which it presents, with the critical remarks which it contains from its able editors, supply one of the best epitomes of current medical literature which it has been our pleasure to read. It is pleasant to be able to congratulate Dr. Head, the general editor of the series, on the excellent way in which the new year has been begun, and we have no doubt but that the subsequent volumes of this series will be as valuable as those which were issued during the year just closed. F. R. P.

PROGRESS

OF

MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF

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The Incidence of Alkaptonuria: A Study in Chemical Individuality.—GARROD (*The Lancet*, December 13, 1902, p. 1616), in a most interesting paper, gives the results of an investigation he has made concerning the blood relationship of the parents of individuals who are the subjects of alkaptonuria. It has now been amply shown that the properties of alkapton urine are due to the excretion of homogentisic acid first discovered by Wolkow and Baumann. The presence of this acid, causes the urine to darken with alkalies and on exposure to air, to stain fabrics a dark brown color and to reduce metallic salts. Its power to reduce copper solutions has led to an incorrect diagnosis of diabetes. Homogentisic acid is derived from tyrosin, but how and where this peculiar chemical change is brought about still remains unknown.

According to most observers alkaptonuria is regarded not as a manifestation of a disease, but rather as an alternative course of metabolism, which is harmless and usually congenital and life-long. This alternative metabolism is considered inferior to the usual plan, owing to a certain slight waste of potential energy. The amount of acid excreted daily varies within rather narrow limits in the recorded cases, the lowest being 3.2 grammes and the highest 5.9 grammes in the twenty-four hours.

The data regarding the incidence of alkaptonuria were gathered from the reports of the 40 cases that have appeared in the literature to date, and also from correspondence with the physicians who recorded the cases. The condition is nearly always congenital. Males are more frequently affected than females, the statistics showing 29 and 11 respectively. The abnormality is apt to occur in two or more brothers and sisters whose parents are normal and among whose forefathers there is no record of its having occurred, a form of incidence seen in other conditions. Thus, in 32 known examples, which were presumably congenital, 19 occurred in seven families. One

family contained four alkaptonurics, three others three, and the remaining three two each.

Garrod's investigation appears to throw important light on the etiology of the condition. In 1901 he pointed out that of four British families in which were 11 congenitally alkaptonuric members no less than three were the offspring of marriages of first cousins who did not themselves exhibit this anomaly. He has carried the inquiry further, and has been able to secure information on this point in 19 of the 40 published cases. He found that 12 of these 19 cases, or more than 60 per cent., were the offspring of marriages of first cousins who did not themselves exhibit this anomaly. This is regarded as being very significant from the standpoint of etiology, and the suggestion is made that this high frequency may be explained by Mendel's law of heredity.

There is only one known instance in which the anomaly has been transmitted by an alkaptonuric father to his son. This case was observed by Osler, the individual being the son of one of the reported American cases. At the present time the condition of the urine of only five children of two alkaptonuric fathers is known. Only one of these children is himself alkaptonuric. That this proportion will be increased on further investigation does not appear probable to Garrod.

According to the writer, the view that alkaptonuria is a chemical "sport," or an alternative mode of metabolism is supported by the study of the incidence of albinism and of cystinuria. In the former males are also more frequently affected, and the offspring of first cousins are particularly liable to the anomaly. In the latter, again, the majority of the cases have been in males, but as yet the evidence of any influence of consanguinity of parents is not abundant. In both, the condition is more likely to occur in the children of parents who do not themselves exhibit the anomaly, thus clearly simulating alkaptonuria. Garrod thinks that it is quite probable that there are other examples of chemical "sports" that have not yet been discovered.

Diabetes Insipidus, with a Report of Five Cases.—FUTCHER (*The Johns Hopkins Hospital Reports*, vol. x. p. 197) reviews at some length the work that has been done on experimental polyuria in animals. In 1849 Bernard showed that there was a point in the floor of the fourth ventricle, just posterior to the Bernard diabetic centre, injury of which caused a simple polyuria. Investigation has shown that injury of other parts of the central nervous system will also give rise to a polyuria.

Clinically there are two classes of cases. First, the primary or idiopathic cases—those in which there is no evident organic basis for the disease. Second, the secondary or symptomatic cases—those attributable to definite organic changes, either of the nervous system or viscera. In some instances it is difficult to decide into which group certain border-line cases should be placed. Some observers classify those cases in which thirst is the first symptom as an independent disease under the name of primary polydipsia. As yet there does not seem to be sufficient evidence to warrant this.

Heredity is an important etiological factor. This is best illustrated by Weil's record of 23 cases among 91 members in four generations of one family. Tuberculosis, syphilis, gout, and general malnutrition were regarded

by Ralfe as important predisposing etiological factors. Tumors involving the medulla and the floor of the fourth ventricle, cerebral hemorrhages, and basilar meningitis are the commonest organic lesions causing the disease. Cerebral syphilis is apparently the etiological factor in a larger number of cases than is generally supposed, the lesion most frequently being a syphilitic basilar meningitis. In one of the five cases here reported syphilis was undoubtedly the cause. The lesion was most probably a basilar meningitis, owing to the history of transitory recurring hæmianopsia which Oppenheim regards as pathognomonic of this lesion. Two other cases were probably also due to a syphilitic infection. A fourth had marked cerebral symptoms, but there was no definite history of lues. The fifth case belonged to the idiopathic group.

From comparative statistics the disease appears less common in this country than in Europe. Only 4 cases, or 0.001 per cent. occurred out of a total of 356,637 patients treated in the Johns Hopkins Hospital and Dispensary. The 5 cases the writer reports were all in males, the ages being 25, 32, 35, 36, and 44 years. The longest duration of the disease in any of the cases was ten years. In all the cases thirst was the first symptom complained of. Four of the five cases had distinctly exaggerated knee-jerks.

The nature of the disease is still uncertain. The only thing that can positively be stated is that it is due to some nervous influence causing a vasomotor disturbance of the renal vessels, leading to persistent congestion of the kidneys. The only constant finding at autopsy is enlargement and congestion of the kidneys. The prognosis is much less favorable in the secondary or symptomatic cases. Treatment is, on the whole, unsatisfactory. In the syphilitic cases anti-luetic treatment should be tried, and sometimes marked improvement in the general health and increase in weight ensues, as was the case in one of the five patients.

Scarlatiniform Erythema in Tuberculosis.—CLAUDE (*Revue de la Tuberculose*, No. 3, September, 1902, p. 261) records an interesting case in which a virulent tuberculous infection was ushered in by a diffuse scarlatiniform erythema of the skin. The patient was a young woman who came under observation on July 28. After having suffered from general malaise, loss of appetite, and muscular pains for a period of seven or eight days, the patient developed an erythematous rash two days before she entered the hospital. It appeared first on the fore-arms, chest, and thighs, and was then patchy. The day after its appearance the patient had a high fever. After admission to the hospital the erythema became general and was of a scarlatiniform type. In five days desquamation began and the rash and desquamation lasted altogether about fifteen days. There was no soreness of the throat, nor any features of the tongue suggesting scarlet fever. The temperature gradually fell to normal by August 11, then it again steadily rose to 40.8° C. before death.

Inquiry showed a family history of tuberculosis. On the day of admission the examination of the lungs was negative. With the disappearance of the rash and the subsidence of the temperature there was not a correspondent improvement in the patient's condition. She gradually emaciated and profuse sweats appeared. Examination of the lungs on August 6 was

still negative, but on August 13 signs of slight dulness, with moist and dry râles, were made out at both apices of the lungs, particularly on the right side. From this date on she failed rapidly and died in coma on August 25.

The autopsy showed an acute miliary tuberculosis involving the lungs, liver, and spleen, bacilli being demonstrated in the tubercles. There were no old foci of caseous tuberculosis found anywhere in the body.

Claude believes that the erythema was a manifestation of an intense intoxication produced by the poisons derived from the tubercle bacilli. He has been unable to find any similar cases in the literature, but says that the scarlatiniform erythema is analogous to that occasionally observed in anginas, diphtheria, and intestinal infections. The writer remarks that not infrequently tuberculin injections are followed by a similar scarlatiniform rash. He comments on the early appearance of the rash, long before any physical signs were present, and regards the eruption as an expression of the virulence of the infection. Owing to its early onset, he designates the eruption as a "pretuberculous scarlatiniform erythema."

Cutaneous Angiomata and Their Significance in the Diagnosis of Malignant Disease.—Symmers (*Medical News*, December 27, 1902, p. 1207) has made a statistical study to ascertain the relationship between cutaneous angiomata and malignant disease. Holländer is credited with having been one of the first, if not the first, to point out this supposed association about two years ago. He believed that the situation of the angiomata was of some importance in determining the location of the malignant disease, holding that capillary angiomata in the gluteal region suggested rectal carcinoma. Leser has recently supported Holländer in his belief that angiomata and malignant disease are intimately connected. He found that 49 patients in a series of 50 cases of cancer had angiomata in greater or less numbers.

Raff examined 500 persons suffering from various diseases and found angiomata in 180, or 36 per cent. Between one and twenty years they were present in 10 per cent.; between twenty and thirty years, in 18.7 per cent.; between thirty and forty years, in 45.3 per cent.; between fifty and sixty years, in 60 per cent.; between sixty and seventy years, in 75 per cent.; between seventy and eighty years, in 88.2 per cent. Raff's results indicated that there was no such association.

Symmers studied a series of 400 cases suffering from all sorts of maladies and came to the same conclusion. Gebele found angiomata in 43 per cent. of a total of 200 cases. He examined 21 cases of cancer and found angiomata in 11, or 52 per cent. Combining Gebele's, Raff's, and Symmers' cases it is found that out of nearly 1100 persons 464, or 42.2 per cent., presented skin angiomata. Symmers made observations in 17 cases of carcinoma and found angiomata in 12, or 76.4 per cent. The angiomata were, however, much fewer than in many of the cases in which cancer was absent. Notwithstanding the frequency in which he found angiomata in his cancer cases, Symmers thinks that they occur too frequently in the non-cancerous cases for them to be of any real value from a diagnostic standpoint.

Symmers holds that some other explanation for them must be sought for. He believes that their presence in persons of all ages is intimately associated

with arterial degeneration. He found in comparatively young individuals who exhibited these skin changes that high arterial tension, and even further signs of precocious arterial sclerosis, were present. In persons between forty and fifty years of age arterial thickening went hand-in-hand with cutaneous angiomata. He, therefore, is inclined to the view that they are an external expression of arterial disease.

(There seems to be no definite relationship between the spider angiomata and disease of the liver. They may appear on the skin of the face and trunk, more frequently, perhaps, in cirrhosis than in any other forms of hepatic disease. See *Johns Hopkins Hospital Bulletin*, 1902.—W. O.)

SURGERY.

UNDER THE CHARGE OF

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The Anastomosis of the Portal Vein with the Vena Cava. A New Operative Procedure.—TANSINI (*Centralblatt für Chir.*, 1902, No. 36) states that the advantage of the diversion of the blood from the portal vein is unquestioned for the relief of certain conditions, and the objection to the method of Talina is that this is accomplished indirectly and not always completely. The author's method has been tried with success on dogs, and consists in an end-to-side anastomosis of the portal vein with the vena cava. Clamps covered with rubber are placed over the veins in order to control hemorrhage, and the portal vein is cut. Then a small spindle-shaped piece of the vena cava is cut out between the clamps, the end of the portal vein is inserted in the opening and the edges closed with silk stitches and the clamps removed. Each one of the dogs experimented upon became fat and was perfectly healthy when killed two months later. Examination at this time showed the union between the veins to be perfect.

The Growth of Bacteria in the Intestine.—SMITH and TENNANT (*British Medical Journal*, December 27, 1902) make the following report of their original work:

The results are of interest because of their bearing on the pathology of a number of diseases. It is clear, as we have shown, that one of the first places in which a disturbance of the regulation of bacterial growth takes place is the region of the ileocæcal junction. The power of inhibiting bacterial growth having become impaired, the bacteria which occur normally in the

large intestine will become still more abundant, and, approximately, similar changes will take place in the small intestine. In the region of the ileocæcal valve the change will occur to a greater extent than in the higher portions of the small intestine. This conclusion follows from a study of the contraction of the relatively sterile area in the small intestine seen in cases of dogs infected with parasites.

In the human subject the region of the ileocæcal valve is very liable to attacks of inflammation in the shape of appendicitis and typhlitis in their various forms, and we are probably near the truth in finding in these diseases an illustration of the mode of bacterial increase which we have just described. Further illustrations of the same principle present themselves in the incidence of the lesions of typhoid fever and tuberculosis of the intestine. It is in the lower end of the small intestine that there occur the earliest and gravest of the structural changes associated with these diseases. We may, therefore, surmise that bacterial invasion of a specific kind follows in these cases the same law as the simple disturbance of regulation due to such non-specific causes as we have investigated. Bacteria possessing specific pathogenic power if taken by the mouth will, like other bacteria so ingested, be restrained from multiplying until the lower ileum has been reached. In other words, the various forms of bacterial irritation of the intestine conform more or less to a type the determining factor of which is the normal power of inhibition of bacterial growth in the small intestine, and in a study of this and the manner in which it is impaired, we obtain important light on the occurrence of these diseases and the tendency which they show to localize themselves chiefly in the lower ileum.

A large number of observations have been made on the bacteria which, though harmless inhabitants of the normal intestine, increase, especially in the small intestine, in various morbid conditions. The principal members of the group are B. coli, B. proteus, various micrococci, and the bacillus enteritidis sporogenes of Klein. When the regulation of bacterial growth is disturbed large numbers of these microbes are found in the small intestine, and they become endowed with increased virulence. In many forms of catarrh of the intestine this increased vigor of bacterial growth is the sole change that can be discovered. The attempt to find a microbe characteristic of such conditions has failed. Again, in typhoid fever, along with the growth of the B. typhi, there occurs an increase in the small intestine of B. coli and other bacteria normally present there. The bacterial change, therefore, which occurs in simple catarrh of the intestine has its place in this disease along with the specific bacterial effects due to the growth of the typhoid bacillus.

It was, as we have already remarked, to enable us to appreciate this part of the pathology of typhoid fever that the present research was undertaken. In the *British Medical Journal* in 1899 we published a paper giving the result of an examination of the serum reactions on a series of typhoid patients. In this we showed that a very considerable percentage of the patients gave not only Widal's reaction, but also more or less pronounced reactions with varieties of B. coli communis. We thus confirmed the observations of Stern, published in 1898, and subsequent investigators have added largely to that confirmation. The interest of this research is that in the B. coli reaction we have a means of obtaining direct proof of the part which B. coli plays in

certain cases of typhoid fever. Long before the evidence of the serum reaction was brought forward it was held by several pathologists that B. coli had a share in the causation of typhoid fever. Various observations on the presence of B. coli in the spleen and other organs of typhoid patients, and Sanarelli's experiments on the influence of coli toxins in raising the virulence of B. typhi had given ground for this conclusion. The study of the regulation of bacterial growth in the intestine which we have just detailed shows, it seems to us, the mode in which normal bacterial processes in the intestine may increase and thereby contribute to a disease without invading the tissues or the blood.

To study this question from another point, we carried out a number of inoculations with races of B. coli, in order to compare the reactions developing in consequence in the animal's (rabbit's) blood with those of the blood of a patient in typhoid fever. This method failed, however, to throw much light on the problem we had before us, but this was probably due to the fact that various races of B. coli differ very much in their reaction to agglutinating coli serums. It often happens that even when a race which does not easily agglutinate is used for inoculation, the resulting serum will give a reaction with other races of B. coli at a dilution much higher than the maximum dilution which will agglutinate the inoculating race. It is consequently impossible to use the serum reaction of the coli group of bacilli in the same definite way as may be permitted with the typhoid group, in which the tendency to agglutinate is much more uniform. There is accordingly an element of uncertainty in interpreting the meaning of coli reaction in a given instance.

Further, in carrying out these inoculations, we tested the rabbit's blood with races of B. typhi, and in confirmation of Sternberg's results, we found that the serum had occasionally acquired the power of agglutinating B. typhi at a dilution at which it had no effect on the B. coli used to inoculate. We do not consider we have yet the data to enable us to interpret this result.

Intracapsular Prostatic Resection. The Normal Method in Cases of Prostatic Hypertrophy.—RYDGIER (*Centralblatt für Chir.*, No. 41, 1902) states that he first recommended enucleation two years ago and that his good results with this method have been equalled by those of Albarran and other surgeons. Further experience with this method has shown that the objection to it is, that no matter whether the enucleation be done with the fingers or with blunt-pointed instruments the prostatic urethra is almost invariably opened. The effect of this is to prolong convalescence, which is undesirable in these cases. For that reason the author now uses the method of intracapsular resection, which avoids this complication by not removing the prostatic tissue lying along the course of the urethra. The technique consists in separating the posterior surface of the prostate from the perineum by a median incision through the raphé. The objection to the half-moon incision between the tuberi ischii is its danger, and its use can only be recommended in very difficult cases. After splitting the perineal fasciæ the prostate should be exposed by blunt dissection. A catheter of as large a size as possible should have been previously introduced into the urethra. The edges of the wound being held apart, the prostatic capsule should be incised on one side of the median

line, and then held apart with retractors while an attempt is made to pull out the prostate with the fingers. This may be easy at times, at others, when the capsule is thin and adherent to the parenchyma of the gland, it may be a very difficult procedure. The urethra being clearly marked by the catheter, the dissection is stopped before it is reached. Clamps are then applied and the prostatic tissue resected. The operation is usually easy, is not accompanied by much hemorrhage, and can be performed in a short space of time in contradistinction to the Dittel operation which, as Buchhardt has aptly stated, is not technically easy, requires about three hours to perform, and is usually accompanied by much hemorrhage. Only further clinical experience can show as to whether the chances of recurrence are greater after one operation than they are from the other, but the chances at present would seem to be about the same.

Two Cases of Obscure Abdominal Pain; Operations; Results.—PRITCHARD (*British Medical Journal*, December 27, 1902) reports the following cases: Case I., woman, aged fifty-three years, had for twenty-three years been subject to intermittent attacks of acute epigastric pain accompanied by vomiting, and lasting, as a rule, for two or three days. The first attack was characterized by jaundice and the usual symptoms of biliary colic, but no calculus was discovered in the stools. There was no history of any illness except an attack of malarial fever. Three months before the operation the patient noticed that her water became highly colored and the motions pale. Soon afterward she began to feel definitely ill; there was considerable pain in the epigastric region, slightly to the right of the median line, and a temperature of 105° F. This temperature soon became remittent and marked jaundice developed. The patient was better one day and worse the next, and as she was steadily becoming weaker an exploratory laparotomy was finally performed, three months after the date of the beginning of her illness. This was absolutely negative in indicating the cause of her condition. The liver and gall-bladder and, in fact, all the abdominal organs were found to be normal in every way. The temperature became normal after the operation and remained so for eight days, but on the ninth day it rose to 104° F., and again another rise five days later. The skin now began to have the peculiar bronze tinge of Addison's disease, and there were patches of almost completely black pigment on the back of the hands and lower parts of the arms. The scar of the wound was not pigmented. The patient was in a very asthenic condition. Believing in the possibility of disease of the adrenals, small doses of arsenic and strychnine were given, and the patient immediately began to improve and in a few weeks was well enough to go home.

Case II.—Woman, aged fifty-seven years, who complained of pain in the right epigastric region, at the level of the junction of the seventh intercostal cartilage. This pain was intermittent, neuralgic, shooting through to the back, and generally at its severest about three hours after a meal. Diet did not affect the severity of the attacks, which were generally accompanied by flatulency. Any vibration, such as riding in a carriage, increased the pain. Rest in bed and medicines having proven of no benefit, an exploratory laparotomy was performed. This showed a mass of fairly dense, fibrous adhesions

connecting the upper portion of the duodenum with the right border of the stomach. The duodenum at its junction with the stomach was kinked at rather an acute angle and there were a few additional adhesions which extended to the free border of the liver and to the structures in the neighborhood. On releasing the adhesions the stomach fell back into its normal position. It was then opened, a rather narrow pylorus freely stretched, and then the wounds were closed. The patient made a rapid recovery and was free from pain for a period of four months, when it returned and was as severe as before and presented similar characteristics.

The Treatment of Cancerous Affections of the Skin by Means of the X-rays.—TAYLOR (*Liverpool Medico-Chirurgical Journal*, October, 1902) reports the following inoperable cases treated by this method: Case I., man, aged sixty-four years, suffering from a rodent ulcer of eight years' duration, affecting the outer canthus of the left eye and lids and the skin, covering the prominence of the malar bone and its orbital prominence. The treatments were given twice weekly with a current of three ampères and a duration of twenty minutes. After eight treatments a reaction set in which was attended by destruction of the newly formed epithelium and surrounding epidermis. The treatment was suspended for three weeks and then resumed when the duration was only five minutes, and in one week the patient was completely cured and has remained so until the present date.

Case II.—Man, aged fifty-nine years, who suffered from lupus erythematosus of the face which was undergoing a spontaneous cure. On his nose, however, was a large, soft, vascular, cauliflower-like growth involving the whole surface of that organ. Nine years previously he had been successfully operated on for epithelioma of the lower lip. As much as possible of the disease of the nose was curetted away, and then the raw surface was submitted to the rays, as in Case I., the other portions of the face being carefully protected with a lead-foil mask. In fourteen weeks the patient was completely well, but lately there has been a slight recurrence on the left cheek. This is improving steadily under treatment.

Case III.—Man, aged eighty-two years, with a rodent ulcer on the side of the nose and at inner canthus, of twenty years' duration. Similarly treated, and the ulcer completely healed in about six months, and as yet there has been no recurrence.

Case IV.—Man, aged seventy-eight years, suffering from a rodent cancer of the left side of the scalp and pericranium of thirteen years' duration. Its dimensions were six inches long by three inches wide. The treatment has been applied during the past twelve months as often as the health of the old man permitted him to attend the hospital. Fully two-thirds of the ulcers are healed, but the disease has spread somewhat posteriorly and over the zygomatic process, and some of the newly cicatrized tissue is breaking down. This case, taken in conjunction with others of a similar character, suggests that the X-ray treatment is not so satisfactory when cancerous affections of the skin involve osseous structures, as when the disease is confined entirely to the soft parts.

In Case V. no escharotic effect was produced, and judging from the other cases the author thought that the results would have been more satisfactory

if it had. In conclusion the author states: First, that the rays are especially indicated in cases of inoperable cancer of the skin. Second, that the best results are obtained when the disease is confined to the soft parts. Third, that, owing to the complete relief of pain and a superior cosmetic result obtained by this treatment, patients too readily assume that they are well before they really are; therefore, they should be warned that a recurrence may take place. In the discussion of this paper Roberts stated that he believed that the effects on the tissues of the skin of the X-rays were, broadly speaking, of two orders: (1) Those of a kind analogous to burning; (2) specific effects. Röntgen rays appeared to exert a specific action on degenerative epithelium. Rodent ulcer was a purely epithelial disease, and there could be no question that the rays caused a dissolution of the new epithelial cells. The same was true of epithelioma and possibly to some extent of other forms of cancer. The remedial influence of these rays on lupus is to be attributed to their burning action and not to any specific influence.

The Treatment of Fractures of the Extremities.—DEBERSAQUES (*Journ. de Chir. and Annales de la Société Belge de Chir.*, 1902, No. 10) states that Sorel has reported excellent results from the ambulatory method of treatment, and the author has tried this method with success in those rare cases of senile fracture of the tibia in children without tendency to displacement; but he does not believe in it for those fractures of the superior segment of the bone. He has obtained excellent results in cases in which the femur is fractured by continuous extension and in children by the use of Schede's apparatus (extension with the member suspended vertically), and so is loth to give up a method which has proven uniformly successful. Sorel has also recommended allowing cases of resection of the knee to walk with an ambulatory splint after the tenth or twelfth day, but the author believes that this is most undesirable and only tends to produce ankylosis.

THERAPEUTICS.

UNDER THE CHARGE OF

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Treatment of Pneumonia.—DR. DYCE DUCKWORTH speaks of the great need for individualization of the treatment of every pneumonia patient. In the main he advocates the use of a mercurial purge in the opening; this may be all the laxative that is necessary. Then a warm bed and careful nursing is of primary importance. For the treatment of the pyrexia he is

not an advocate of the use of ice bath or of any of the newer antipyretics. Quinine, he finds, fills every indication for pyrexia, and this he administers in 5-grain doses every two, three, or four hours until the reaction takes place. Fluid extract of cinchona may be used alternately with the quinine. A mild saline may be added. On the question of the use of opium in pneumonia he is more for than against, especially for those patients in whom there is no indication of kidney changes. A good plan is to give morphine in small doses with a suitable vehicle, preferably compound spirit of ether. As for the heart failure condition, in the acute engorged pulmonary areas with cyanosis, or even jaundice, he sees an indication for venesection, withdrawing as much as twelve ounces of blood. If the heart begins to falter and the pulse becomes irregular and small, give oxygen and do not put it off until late in the disease. Ten-minute intervals are sufficient. Strychnine is recommended. Digitalis he does not think so serviceable as strychnine. Musk is also advocated. Tincture of musk with Hoffman's anodyne makes an excellent mixture. Two or four ounces, or even more, of brandy a day will prove of service.—*British Medical Journal*, 1902, No. 2188, p. 1573.

Action of Heroin and Dionin on Respiration.—Dr. C. R. Marshall makes a contribution from a scientific standpoint on the action of these two morphine derivatives. From the standpoint of the pharmacological relation to the chemical formula of these drugs the inference has been drawn that dionin more closely approximates morphine in its action than heroin. It is more sedative to the nerve structures than heroin, is less convulsant, less active on the respiratory centre, and less toxic. Compared with morphine it is less toxic, less sedative, more convulsant, and less depressant to the respiratory centre. Heroin compared with morphine is much more toxic, much more convulsant, and much more active to the respiratory centre. Since the action of these two drugs, particularly on the respiration, is in need of thorough investigation, conclusions are well worth recording. He finds that heroin can prolong inspiration and increase the depth of respiration, but that the limits of its beneficial action, unless simple slowing is required, are soon passed. Slowing is always produced. In moderate doses it depresses the respiratory centre. Dionin appears to be slightly more sedative than codeine, but otherwise it possesses the same action. Heroin has a much greater effect on the respiratory centre, an action which has been compared to the action of digitalis on the heart.—*British Medical Journal*, 1902, p. 1219.

Injections of Yolk of Egg for Tuberculosis.—Dr. T. Bayle makes the ingenious suggestion to use the yolk of egg, rendered more fluid by equal parts of physiological salt solution, by hypodermic injection for the treatment of tuberculosis. At least an ounce may be introduced without fear of setting up a local irritation. The results are claimed to be excellent in those cases of deficient alimentation from severe gastric disturbance. The author holds that the lecithin which is normally present in large amounts in the yolk of the egg is not subjected to the molecular breakdown incident to its passage through the digestive process. The procedure is contrain-

dicated when the digestive processes are normal. The author holds that the lecithin of the yolk is more stable than any of the heretofore produced lecithin on the market. Injections should be made of sterile material subcutaneously.—*Lyon Médicale*, 1902, No. 14, p. 427.

Pseudaconitine and Japaconitine.—Dr. J. Theodore Cash, in a study of these alkaloids related to aconitine says that, used inwardly, pseudaconitine and japaconitine given in the proportion indicated (pseudaconitine, 0.4 to 0.45; japaconitine, 0.8 to 0.9, the dose of aconitine) may be employed for modifying circulatory activity in some febrile states, for the relief of pain, and for other purposes which have been answered by the exhibition of aconitine. It may be added that solutions of the alkaloids would be very preferable for employment to preparations of the plants which yield them, for in the latter the main alkaloids not only vary in proportion but are often associated with other principles which have a somewhat neutralizing or qualifying effect. For local relief of pain the three alkaloids have been found to act well in similar proportions (2 per cent. to a basis of oleic acid and lard in the British Pharmacopœia being the proportions employed). When the use of such a potent preparation is contemplated it is essential that the cutaneous surface should be sound and free from abrasion.—*British Medical Journal*, 1902, No. 2181, p. 1243.

Mannitol Pentanitrate.—Drs. C. R. Marshall and J. H. Wigner conclude a series of studies of this new vasodilator as follows: It is evident from the sphygmographic tracings that mannitol pentanitrate is less active than erythrol tetranitrate, but much more active than mannitol hexanitrate. It would undoubtedly prove a useful drug if erythrol tetranitrate were unknown, but its only great advantage over this substance is its relative cheapness when prepared on a large scale. It can, however, in double the dose produce all the effects of erythrol tetranitrate. It can as readily be obtained pure, and it is somewhat more stable. It possesses the usual ill-effects of the organic nitrates—slight heaviness and tendency to headache, and it also has a bitter taste. Pharmacologically, it is very interesting, but its mode of action and certain other points we must leave to a future communication. The second objection to erythrol tetranitrate is its explosiveness. When rapidly heated, sometimes when struck, it detonates and disappears. If handled with ordinary care, however, it is quite harmless. It can be made perfectly so by mixing it with oil of theobroma, which is easily done by melting and then converting this into tablets. And this, besides being the best form, ought to be the most economical, as it is unnecessary to crystallize the nitrate previous to mixing it with the cocoa-butter. Mannitol pentanitrate, in this respect, possesses advantages over erythrol tetranitrate, since it is more stable and much more soluble in oil of theobroma.—*British Medical Journal*, 1902, No. 2181, p. 1231.

Treatment of Graves' Disease.—Dr. M. Schultes has made a series of investigations on the action of a serum obtained from sheep or dogs from which the thyroids have been removed, following the initial suggestion of Ballet and Enriquez. He reports the case of a woman, aged forty-two

years, who had had exophthalmic goitre four years. Palpitation, anxiety, and delirium were prominent symptoms. The exophthalmos was marked, the thyroid much enlarged, the circumference of the neck being seventeen inches. The initial dosage of this new body as prepared, termed antithyroidin, was 7½ grains. This was increased until she was taking 70 grains three times a day. After two weeks her delirium was markedly improved, the pulse rate had dropped to 100, the circumference of the neck diminished almost an inch. A week later the pulse rate was 88, the thyroid was softer, and the patient was able to attend to light work, such as sewing, from which she had been deprived by reason of the marked tremor. After seven weeks she was sufficiently better to be termed well.—*Münchener medicinische Wochenschrift*, 1902, No. 20, p. 834.

Hypodermic Purgatives.—Dr. Walter E. Dixon says that a drug that can be introduced subcutaneously and produce a purgative effect is a want distinctly felt in medicine. Such a body would be of the greatest advantage in a variety of conditions, such, for example, as inflammation of the stomach where a purgative action was required, in apoplexy and unconsciousness from other causes, and after certain abdominal operations. In spite, however, of this want, pharmacologists have not succeeded in introducing a suitable substance, and although many drugs producing the desired effect have been suggested, yet these have invariably been found to give rise to conditions which prohibit their use in the form of an injection. For convenience of description, drugs producing a purgative action on injection may be divided into four groups. These he divides as vegetable purgative, salines, drugs acting peripherally, and drugs of the morphine series. Of this latter group he draws attention to the following facts with regard to apocodeine. It lowers blood pressure, produces vasodilatation, and increases peristaltic movements—all probably as a result of its sedative action on the sympathetic inhibitory ganglia. It does not produce vomiting or give rise to other ill-effects, and he therefore hopes that it will receive an extensive trial as a hypodermic purgative. Finally, he suggests that a 1 or 2 per cent. solution of the hydrochloride be used, which should be neutral and filtered before use. Thirty to forty minims may be injected for a dose.—*British Medical Journal*, 1902, No. 2181, p. 1245.

Phenolphthalein as a Purgative.—Dr. F. W. Tunnicliffe gives an interesting résumé of the so-called synthetic purgatives, and discusses the relation of the various anthracene cathartics from a chemical standpoint. Phenolphthalein comes in for special study, concerning which he concludes that: 1. For children, phenolphthalein in doses of from ¾ grain to 2¼ grains is a useful aperient. 2. For ordinary adults this drug must be given in doses of from 1½ grains to 4½ grains. 3. In cases of obstinate constipation the dose must be increased to 15 grains. 4. Phenophthalein produces purgation in jaundice. It has no irritating effects on the kidneys; its depressant action on the circulation is less than that of magnesium sulphate. —*British Medical Journal*, 1902, No. 2181, p. 1225.

OBSTETRICS.

UNDER THE CHARGE OF

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The Result of Total Suppression of Urine in Pregnant and Non-pregnant Animals.—Blumreich (*Archiv für Gynäkologie*, 1902, Band xlvi., Heft 2) has previously made a series of investigations to determine whether increased sensibility is characteristic of the nervous system during pregnancy. His experiments were conducted by injecting creatin into the brain of pregnant animals after trephining, and in the second group of cases by injecting a solution of creatin into the blood current through the carotid artery. His results demonstrated the fact that in pregnant animals a condition of increased sensibility to reflex irritation is found in the nervous system.

This is corroborated by clinical observation, which shows that eclampsia, tetanus, and chorea are found with special frequency in pregnant patients.

In order to determine as nearly as possible the source of the irritating material causing eclampsia, Blumreich experimented upon pregnant and non-pregnant animals, by causing complete retention of urinary excreta by extirpating both kidneys. This operation is performed without much difficulty by placing the animal upon the abdomen, and under anæsthesia, making an incision along the back at the eleventh vertebra, in such a position that both kidneys can be readily removed through one incision. The first animal operated upon died from peritonitis through an accident which opened the peritoneal cavity; the others showed no evidence of infection. Ten pregnant animals and twelve non-pregnant were operated upon. In most of the cases rabbits were used.

There was no immediate effect following the operation. The animals moved about freely and ate with appetite. The first evidence of disease was increased irritability, so that the skin could not be touched or stroked without causing great uneasiness. Convulsions in groups of muscles then followed, with drawing of the head backward and toward the right side. In some cases clonic convulsions occurred. This gradually extended until most of the muscles of the body were involved. They resembled those which followed the injection of a solution of creatin into the carotid artery.

The nervous system showed not only increased excitability, but very soon in the progress of the case an anæsthetic effect was noticed. The animals not only ran about eagerly, but at times lay quietly, as if anæsthetized.

In non-pregnant animals convulsions began, on the average, 71 hours after the operation. Death occurred on the average 79 hours after the operation. In pregnant animals convulsions occurred in 63.4 hours after opera-

tion, and death followed the operation, on the average, in 70.8 hours. The shortest period in which convulsions occurred after operation was 40 hours the longest, 104 hours.

Further experiment was made by feeding two groups of animals—one pregnant, the other non-pregnant—operated upon, with the same food, when it was found that the difference in the frequency and prompt occurrence of the convulsions between pregnant and non-pregnant animals is very much lessened.

The conclusions drawn from these experiments strengthen our belief that the brain of the pregnant animal is more sensitive to irritation that that of the non-pregnant. The substances which produce convulsions exist essentially in the non-pregnant as well as in the pregnant.

One fact stands out very clearly from these and other experiments upon this subject: eclampsia is not the result of uræmia. While lesions in the kidney may assist in producing eclampsia, these lesions are the result of the circulation of poisons which in themselves cause eclampsia. Experiments show that animals, whether herbivorous or carnivorous, generate poisons in the body during pregnancy. To isolate poisons which produce eclampsia it will be necessary to isolate from the blood, the central nervous system, or the urine substances which are capable of exciting irritation in the nervous system during pregnancy.

Tubal Gestation.—In the *Journal of Obstetrics of the British Empire*, June, 1902, CHAMPNEYS contributes an interesting paper upon this subject, with the results of his study of seventy-five cases of tubal gestation from the wards of St. Bartholomew's hospital.

He calls attention to the fact that more than twenty years ago these cases were diagnosed as hematocele, while later the same cases were called perimetritis. Before 1893 the diagnosis of ectopic gestation was not very commonly made. From 1865 to 1877 there were at St. Bartholomew's Hospital 129 cases in which hematocele was diagnosed, and of these five died, a mortality of nearly 3.87 per cent. During the next two years the mortality remained the same, but a smaller number of cases were diagnosed as hematocele. From 1891 to 1900 there were thirty-six cases of hematocele, of which none died. During the first twelve years the diagnosis of ectopic gestation was made six times, with one death. During the second twelve years it was made in ten cases, with two deaths; and during the next nine years in sixty-three cases, with nine deaths.

Champneys practises and teaches the following principles of treatment in these cases:

1. Cases of early, unruptured, living, tubal gestation should be operated on without delay.

2. Cases of rupture into the peritoneal cavity, with diffuse hemorrhage, should be dealt with according to circumstances.

(*a*) If hemorrhage still continues when they come under observation some cases ought to be subjected to operation, taking into consideration the probability of the limitation and encapsulation of the blood continuing and the state of the patient at the time.

(*b*) If seen after hemorrhage has ceased they should be treated expectantly.

3. Cases in which the blood has been encapsulated by adhesions or by the broad ligament should be treated expectantly, and operated on if pregnancy appears to be progressing.

4. Hematoceles which refuse to be absorbed in a reasonable time should be opened, emptied, and drained.

In explanation of these propositions it is recognized that it is very difficult at times to diagnose an unruptured tubal gestation. Regarding those cases which rupture into the peritoneal cavity, the death of the ovum immediately occurs; hence it ceases to be a source of danger. If the patient recovers from the shock she usually survives the accident. To operate during the stage of shock he believes is in many cases to kill the patient; to operate after the shock has ceased is usually unnecessary.

Champneys adds detailed reports of seventy-five cases which have been under his personal charge in St. Bartholomew's. The mortality of these cases was seven, or 9.3 per cent.; 45.3 per cent. of these cases were left alone, and recovered; in 20 per cent. vaginal section was done, without mortality; in 65.3 per cent. nothing was done as soon as the patient was admitted or during the active stage of hemorrhage, but later on vaginal section was performed. Immediate abdominal section was done in but 12 per cent. of the cases. Secondary abdominal section was done in 22.6 per cent., and abdominal sections, both primary and secondary, in 34.9 per cent. There were forty-nine cases, or 65.3 per cent., in which abdominal section was not done.

The mortality of vaginal sections was nothing, and the mortality of abdominal sections, primary and secondary, was 26.92 per cent. Primary abdominal sections gave better results than secondary. In the former the mortality was 22.2 per cent., and in the latter 29.41 per cent. The mortality of all abdominal sections in these cases was 9.3 per cent., or that of the entire series. Four cases were opened through the vagina under a mistaken diagnosis. Five cases were possibly operated upon too late, and there were two cases in which abdominal section was superfluous. There were twelve cases in which the tumor was larger than a cricket-ball, and three cases in which the tumor increased after admission to the hospital, but which recovered without operation. In four cases there were attacks of pain without increase in the tumor, and in two cases the hematocele was discharged through the rectum. Champneys calls attention to the fact that rise of temperature does not necessarily indicate infection of the sac.

He does not have resort to mere puncture. When opening such a tumor through the vagina he cuts through the vaginal wall, stopping any bleeding before proceeding further, and opening the cyst with the fingers, aided with some blunt instrument. After washing out the sac he is accustomed to drain with gauze.

In summarizing these cases Champneys calls attention to the fact that 60 per cent. of the whole number recover without abdominal section.

Duration of Lactation.—In *L'Obstétrique*, May 15, 1902, PLANCHON contributes a paper upon the duration of lactation, in which he describes various conditions in which lactation has continued under unusual circumstances.

Of 245 patients who consulted him before their children were seven months old, 158 were not nursing children, 78 had not had sufficient milk for a nursing child, and 14 had no milk at all.

Among the causes for interruption of nursing he places, first, inflammation of the mammary glands, with breast abscess, strong mental disturbance and violent emotion, sudden failure of the kidneys, affections of the heart, and the appearance of menstruation in the nursing mother. The number of nursing mothers in whom menstruation returned is variously estimated at from 39 to 43 per cent. Observation shows that in women nursing a child, should menstruation occur, the quantity of milk is distinctly lessened and its quality impaired during menstruation.

Among these patients but two were found who were able to nurse a child as long as fourteen months; 63.6 per cent. had sufficient to nurse a child for seven months, 55.3 per cent. for eight months, 37.8 per cent. for nine months, 22.7 per cent. for ten months, 13.6 per cent. for eleven months, 6 per cent. for twelve months, and 1.5 per cent. for thirteen and fourteen months.

The Production of Eclampsia. In the *Archiv für Gynäkologie*, 1902, Band lxvi., Heft 2, MÜLLER contributes an extensive and interesting paper upon this subject.

Reviewing thoroughly the literature of the subject, he concludes that eclampsia is the result of a general and systemic poison. The place of origin for this poison he believes to be the interior of the genital tract, and especially the interior of the uterus. Reasoning by analogy, he concludes that the same or analogous causes which produce fever during pregnancy and labor produce eclampsia also. He bases this decision upon a careful comparison of those complications of pregnancy and labor resulting in fever with the conditions which precede eclampsia. He finds that so far as the fœtus is concerned both fever and eclampsia greatly jeopardize its life. He draws a close parallel between all of the circumstances attending fever in pregnancy and labor with those which result in eclampsia.

He believes that necrosis of the decidua, with the presence and activity of bacteria, produce eclampsia. He calls attention to the fact that eclampsia is most frequent as the intra-uterine tension increases through the progressive growth of the ovum.

His suggestions for treatment are to empty the uterus promptly, taking special care to remove the decidua and all portions of placenta and membranes. So far as the prophylaxis of eclampsia is concerned, nothing can be done except to keep the patient as clean as possible.

[This paper is chiefly valuable for the excellent review which it contains of the literature of the subject. It is hard to reconcile the writer's theory with facts observed through clinical observation. If the interior of the uterus is the source of the poison-producing eclampsia, why should a restricted diet diminish the danger of eclampsia? If the only available treatment is the complete emptying of the uterus, why is it that many patients do best when the uterus is not emptied until nature gradually accomplishes this, while the patient is made to eliminate freely by packs, baths, and other means. We are quite agreed with the writer that eclampsia is the result of systemic poison, but we must have further evidence before we can accept his statement that the genital tract is the source of this poison.]

Cæsarean Section for Placenta Prævia.—In the *Boston Medical and Surgical Journal*, June 12, 1902, CONROY reports the case of a multipara whom he found bleeding profusely from placenta prævia. On examination the os uteri admitted the finger-tip, and the placenta was felt completely covering the orifice. The vagina was tamponed with cotton, and stimulants given hypodermically, and consultation summoned. On further examination it was found that the tampon was not controlling the hemorrhage, and the patient was delivered by Cæsarean section. The child was stillborn, and had apparently been dead for some hours. The mother made a good recovery.

GYNECOLOGY.

UNDER THE CHARGE OF

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Hot Air in Gynecological Treatment.—POLANA (*Centralblatt für Gynäkologie*, No. 37, 1902) commends highly Bier's method of steaming, especially in cases of old pelvic exudates. A Ferguson's speculum is introduced if it is desired to produce a direct effect upon the vaginal fornix or uterus. The treatment is also useful in hastening the development of abscesses, also for assisting the healing process after they have been incised per vaginam.

Since the effect of the heat is to increase uterine congestion, its use is contraindicated in endometritis, while it is of value in cases of amenorrhœa and imperfect development of the pelvic organs. The presence of any elevation of temperature is an absolute contraindication.

The writer does not claim that this treatment is followed by an anatomical cure, but that patients with obstinate chronic trouble are permanently relieved of their pain.

Fibromyoma Complicated with Pregnancy.—BAECKER (*Centralblatt für Gynäkologie*, No. 38, 1902) in reporting six cases states his belief that in spite of the fact that the tumor is benign, pregnancy in a fibroid uterus is a condition which is fraught with danger, during both the pregnancy and the puerperium, varying according to the size and location of the neoplasm. Before the third month it is advisable to empty the uterus in a doubtful case. After the third month expectant treatment should be followed, but if serious complications arise the writer prefers hysterectomy to a palliative operation, which may expose the patient to the risk of fresh danger from a subsequent pregnancy. Hence, he does not approve of enucleation, even when combined with castration. Of course, the intelligent consent of the patient to a radical operation is necessary.

Laparotomy during Pregnancy.—MARSCHNER (*Centralblatt für Gynäkologie*, No. 38, 1902) reports the case of a multipara, aged thirty years, who entered the hospital with the diagnosis of extrauterine pregnancy, as she had skipped two periods and was suffering from severe abdominal pains. On examination under anæsthesia the uterus appeared to be small and an adherent tumor was felt on the right side. Hegar's sign was absent. Opening the abdomen, the writer found that the pregnant uterus was retroflexed and firmly fixed by fundal adhesions. A small fibroid attached to the lower segment was removed after the adhesions were separated. The convalescence was normal, the patient was discharged on the fifteenth (!) day, and was delivered subsequently at full term.

The same writer reports the following cases of pregnancy complicated with fibroid:

CASE I.—A multipara, aged thirty-five years, who had been in good health since her previous pregnancy ten years before, when three months advanced in her second pregnancy was suddenly seized with severe abdominal pains, accompanied with chills, fever, and tympanites. The diagnosis of pregnancy complicated with fibroid tumor and peritonitis was made, and abdominal section was performed. A suppurating fibro-myoma was removed with difficulty, pus escaping freely, while the hemorrhage was profuse. A large, raw surface on the uterus was sutured with deep catgut and superficial silk sutures. No drainage was used. The convalescence was stormy—uncontrollable vomiting for five days, intestinal paralysis for a longer period, and, finally, obstinate coughing. On the eighth day the upper angle of the wound burst open and omentum prolapsed, so that a second operation was necessary on the twelfth day. Following the second anæsthesia there was obstinate vomiting as before. In spite of all these complications the patient recovered, the pregnancy continued, and she was delivered normally at term.

CASE II.—The patient, aged twenty-nine years, denied pregnancy, but had missed four periods, and was in a miserable condition when she was admitted, suffering with severe abdominal pains. The uterus was as large as a child's head, and was studded with myomatous nodules. On opening the abdomen it was found to be impossible to perform a conservative operation, so that the whole mass was removed, the patient having a normal convalescence.

These cases illustrated another complication of pregnancy:

CASE I.—A multipara, aged thirty-nine years, entered the hospital with chills, fever, abdominal pain and tympanites. Pregnancy at four or five months was recognized. The cul-de-sac was filled with a soft tumor, which was supposed to be a suppurating dermoid cyst. This was confirmed by vaginal section. The contents of the cyst were evacuated, and the sac was removed with great difficulty on account of firm adhesions, it being necessary to manipulate the uterus considerably. Gauze drainage was used. In spite of the rough usage of the pregnant uterus the recovery was normal, and the patient completed her full term.

CASE II.—A young woman, early in her fourth pregnancy, had suffered for a month with irregular hemorrhages, backache, nausea, and vertigo. A retroflexed uterus was replaced and supported by a pessary, but the pain

and hemorrhages continued. A movable ovarian cyst, the size of an egg, was discovered and operation was advised on account of the danger of torsion of the pedicle. This was easily effected, the unpleasant symptoms promptly disappeared, and the subsequent course of the pregnancy was uneventful.

Anatomy of Chronic Parametritis.—FREUND (*Centralblatt für Gynäkologie*, No. 43, 1902) presents the results of his recent studies bearing on this subject, which confirm his previous views with regard to the relation of this condition to certain reflex nervous symptoms. Sections through the diseased tissues show marked changes in the pelvic ganglia included within them. Besides being surrounded and compressed by the cicatricial tissue, their cells are shrunken, lose their normal shape, and the nuclei mostly disappear. The writer believes that this subject offers a fruitful field for investigation, and that various reflex neuroses usually referred to hysteria may be explained by these changes in the intra-pelvic ganglia.

Diagnosis of Genital Tuberculosis.—SELLHEIM (*Centralblatt für Gynäkologie*, No. 43, 1902) believes that the probable tubercular character of obscure pelvic disease in an individual may be inferred if it is present in other organs, or in members of the same family. If isolated nodules can be detected in the pelvic peritoneum, and especially at the uterine end of the Fallopian tube, the diagnosis is almost certain. The tube has a characteristic rosary-like feel, the nodules being of firm consistence.

Curettement of the uterine cavity and microscopic examination of the tissue removed should never be omitted in cases of suspected tuberculosis of the tubes and pelvic peritoneum, since in this way important information may be obtained bearing upon the questions of prognosis and treatment. If such a thorough examination is made the writer believes that in the majority of cases it is possible to make a diagnosis of genital tuberculosis.

He reports sixty-five cases observed at the Freiburg clinic in the course of eight years; twenty-eight of these were treated palliatively, with satisfactory result as regards the relief of symptoms and arrest of the disease; thirty-seven capital operations were performed, with equal success. Total extirpation of the uterus and adnexa is preferable.

Treatment of Pelvic Suppuration.—JUNG (*Centralblatt für Gynäkologie*, No. 43, 1902) reports 122 cases of laparotomy from the Greifswald clinic, with a mortality of 18 per cent., which he explains by the fact that these included the worst cases, small pus tubes and ovaries, with slight adhesions, being removed per vaginam. Another explanation of the high death rate was afforded by the virulence of the pus, which was found to be sterile in only 14 out of 78 cases in which it was examined bacteriologically. Streptococci were found twenty-six times, gonococci twelve times, colon bacilli six times, and tubercle bacilli thirteen times. Vaginal section and drainage are now practised at the clinic, the diagnosis being greatly aided by examination of the blood. In 21 recent cases the patients were cured by this method.

Treatment of Retroflexion.—WINTERNITZ (*Centralblatt für Gynäkologie*, No. 43, 1902) recognizes four classes of cases, viz.: 1. Uncomplicated movable retroflexion in multiparæ, the symptoms being mostly nervous and not due to the local condition. Such patients should not be treated at all. 2. Simple retroflexion in women who have borne children, but have no laceration of the pelvic floor. The displacement may be corrected by a pessary or by operation. 3. Retro-displacement and prolapsus from loss of the pelvic floor, accompanied by the usual dragging symptoms. Here an operation is indicated, really to correct the prolapsus. 4. Complications on the side of endometritis, diseased adnexa and adhesions, where the retroflexion is a side issue and surgical treatment is clearly indicated.

Diabetes in Gynecological Operations.—FÜRTH (*Centralblatt für Gynäkologie*, No. 43, 1902) lays down the following rules with regard to operations in diabetics: 1. Reduction of the amount of sugar by strict diet and the administration of soda. 2. Removal of all mental excitement as far as possible, and relief of pain without narcotics if this can be effected. 3. Strict attention to asepsis and antisepsis. 4. Avoidance of exhaustive purging and loss of fluid from the system, an enema being given the night before the operation, which should be performed early in the morning. 5. Local or lumbar anæsthesia is preferable to general narcosis. 6. Saline enemata should be given after operation, citrate of soda being administered as before, with easily digested food. 7. If the convalescence is smooth, massage should early be practised.

OPHTHALMOLOGY.

UNDER THE CHARGE OF

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Ablation of the Crystalline Lens to Rectify High Myopia.—SIR WILLIAM J. COLLINS, London (*Lancet*, December 13, 1902), reports nine cases of high myopia, twelve to twenty-three D., operated by himself. In all the nine cases there was some improvement of vision and in some very great. In no case was the operation followed by untoward symptoms. His conclusion is that "the operation in suitable cases—a limited class—is so reasonably safe and attended often with such brilliant results, that it should be regarded as a recognized procedure in the treatment of high or advancing myopia in young persons."

Optic Neuritis in Diphtheria.—BOLTON, London (*Lancet*, December 13, 1902), reports two cases of this very rare complication of diphtheria. While

optic neuritis is well known in the toxæmias due to Bright's disease, lead, syphilis, and chlorosis, and has been described in certain acute specific diseases as enteric fever, influenza, mumps, and scarlet fever, it is surprising not that optic neuritis should occur in the toxæmia of diphtheria, but that it is so rare. In fact, the reporter after searching the literature was not able to find a single case recorded, though Fromaget describes a case of post-diphtheritic amblyopia due, as he thinks, to retrobulbar neuritis. In Bolton's cases the disease was binocular; in the first case the neuritis appeared during the fourth week, in the second case probably about the third or fourth week. In both cases the knee-jerks were absent, and palsies of some distant muscles existed. The inflammation subsided in about two months.

When to Operate for Senile Cataract, the Other Eye Possessing Useful Vision.—KEIPER, Lafayette, Ind. (*Annals of Ophthalmology*, October, 1902), has addressed over a hundred members of the Section of Ophthalmology of the American Medical Association upon the question of removing a ripe senile cataract when the other eye has useful vision, and as to the complaints of the resulting anisometropia. The views of the gentlemen addressed were somewhat at variance. The majority, however, favored operating under the given circumstances. Keiper urges the operation because of the increased field, avoidance of hypermaturity, absence of a period of blindness, greater comfort, and improved appearance. The aphakic eye should not be corrected so long as the other eye has the more satisfactory vision.

Softening about the Right Calcarine Fissure Associated with Left Hemianopsia.—PERDRAU, London (*Edinburgh Medical Journal*, January, 1903), describes the case of a female, aged sixty-nine years, suffering from dementia. She was unable to recognize anyone approaching her from the left, but was immediately conscious of objects appearing on her right. Perimetric observations showed that she had left hemianopsia. Death occurred in coma in a few months. The section showed that there was a small area of softening at the apex of the right cuneus and adjoining portion of the lingual convolution, the proper nervous tissue being replaced by connective tissue rich in cells.

The softening was due to thrombosis occurring in the right internal parieto-occipital artery, which was markedly atheromatous.

The Treatment of Phlyctenular Keratitis.—MARSHALL, London (*Practitioner*, January, 1903), thinks that iron, the remedy most commonly prescribed in the phlyctenular keratitis of children, is frequently injurious. The extreme irritability of the eyes is aggravated by its use in the early stages, while it is useful enough at a later period. In the early stages it is far better to employ mercury internally. This may be advantageously exhibited in the following combination from the Moorfield's *Pharmacopœia:* Gray powder, grain j; powdered belladonna leaves, grain ss; sugar of milk, grain j. One powder twice daily.

Atropine locally is essential with frequent bathing in boracic lotion. Later, but not in the acute stage, an ointment of the yellow oxide of mercury, two to eight grains to the ounce, is useful. At this stage iron is indicated.

For the photophobia all sorts of measures have been recommended—blis-

ters, setons, insufflations of calomel or powdered glass (!), and holding the child's head under water. None of these are to be thought of. The development of fissures and excoriations at the outer canthi is one of the chief causes of the photophobia, cure of which is half the battle. The best treatment is stretching the fissures so as to make them bleed, preferably under an anæsthetic. At the same time they may be painted with a solution of nitrate of silver, five to ten grains to the ounce. Cocaine, though it may be of great use in aiding the surgeon to make a thorough examination, should never be given to the patient; neither should alum nor sulphate of zinc. All three of these agents tend to destroy the epithelium and favor perforation.

Restoration of Sight in a Nearly Blind Cancerous Eye by Cancroin.—ADAMKIEWICZ, Vienna (*Medicine*, January, 1903), reports the case of a woman, aged forty-two years, twice operated upon for cancer of the right mammary gland. About a year after the second operation the left eye became the seat of a cancerous infiltration of the choroid, with partial detachment of the retina. Vision was reduced to light perception. At this time the operative cicatrix showed recurrence, with involvement of the lymphatic glands. Cancroin injections were now commenced. On the day following there was distinct diminution in the infiltration of the scar. On the third day the enlarged clavicular gland was diminished in size. Rapid improvement continued. Improvement in the vision began from the moment of the injections. The day following the first injection there was an improvement in the periphery of the field of vision, and the hand could be recognized with the fingers separated ten inches from the eye. After the eighth injection the sight of the left eye improved so that the field of vision had two-thirds of the normal area. Sight had returned in the lower temporal quadrant of the retina, which was not detached, but was probably the site of a cancerous infiltration. The cancerous infiltration elsewhere seemed to have disappeared. The patient at this time suspended treatment.

PATHOLOGY AND BACTERIOLOGY.

UNDER THE CHARGE OF

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Cyst of the Pancreas.—CHEVASSU and THENVENY (*Bull. et Mém. de la Soc. Anat. de Paris*, 1902, vol. i., iv., p. 205). The authors describe a cyst in the tail of the pancreas occurring in a woman, aged forty-three years. It could

be felt in the left flank, and appeared the size of two fists. The tumor had probably existed for at least twenty years. Laparotomy was performed and the mass removed. It proved to be a cyst about the size of a fist, having irregular walls and being filled with 300 grammes of a sanguinopurulent fluid. Microscopically the cyst wall was lined with high columnar epithelium, alternating with small projections composed of ducts of cuboidal epithelium, the same duct-like structures being present in the connective tissue walls. The authors suggest that the cyst was of embryonic origin and are inclined to class it with the embryonic cysts of the ovary, testicle, and thyroid gland.—W. T. L.

The Passage of Tubercle Bacilli into the Lymphatic and Thoracic Duct after Ingestion.—NICOLAS and DESCAS (*Cent. f. Bakt. u. Parasit.*, 1902, vol. xxxii. p. 306). Large numbers of tubercle bacilli were suspended in a fatty broth and fed to dogs. In a certain number of cases, after three hours, tubercle bacilli were present in the thoracic duct in such great numbers that they could be demonstrated in stained smears, and by inoculating the chyle into animals tuberculosis could be produced. The authors point out the importance of these results, although somewhat limited, as an explanation for the development of generalized tuberculosis arising by way of the alimentary passages.—W. T. L.

Experimental Investigations upon the New Formation of Inflammatory Granulation Tissue.—ALEXANDER MAXINOW (*Beiträge zur Path. Anat. u. zur Allg. Path.*, Fifth Supplement, 1902). Maxinow has studied experimentally the formation of granulation tissue by introducing sterilized foreign bodies into the subcutaneous tissues and intermuscular tissue of rabbits and dogs. For this purpose small glass plates and celloidin sacs were generally used. Examinations were made of the inflammatory products in both fresh and hardened preparations. Maxinow believes that the cells making up the greater portion of the granulation tissue retain throughout their development a certain specific character and perform definite functions in the general process of tissue repair. The first cell to appear after the introduction of the foreign body is the polymorphonuclear leucocyte, the specific granulated cell of the blood. These cells wander from the vessels and presumably prepare the tissue in some way for the succeeding invasion of other cells. In aseptic conditions the leucocytes show little or no phagocytic action. They soon disappear or degenerate where they lie. The fibroblasts are the true forerunners of the new connective tissue, and are derived entirely from the pre-existing connective tissue cells. They are, moreover, highly differentiated cells, and cannot exist in certain locations where both leucocytes and polyblasts show definite development. They are capable of movement. In rabbits they are never phagocytic, in dogs phagocytosis is sometimes observed. The collagen fibres or intercellular substance is the later product of these cells. The new capillaries are formed by a proliferation of the endothelial cells of pre-existing blood-vessels. The capillary endothelium represents a highly differentiated type of cell, and its multiplication is devoted solely to the formation of new

bloodvessels. One of the most important cells is that called by Maxinow the polyblast. This cell is the small lymphocyte of the blood, which, according to Maxinow's researches, is identical with the lymphoid cell found in the connective tissues and the clasmatocytes and clasmatocyte-like cells of the adventitia of small vessels. The polyblast is capable of motion, and shortly after the introduction of foreign substances into the tissues, great numbers of these cells wander from the bloodvessels and enter the surrounding tissues. The fixed cells also enter into this invasion, although they form comparatively but a small portion of the total number of polyblasts. After their escape from the vessels the polyblasts undergo various changes. They may become larger and assume phagocytic properties, and are then identical with the well-known phagocyte of epithelioid cell; or they may take on a form similar to the fibroblast, and when they lie between fibroblasts they are in some instances actually capable of producing connective tissue, although this does not seem to be their primary function. When the young polyblasts penetrated into the cavity of the foreign bodies their different stages of development could be traced during the growth of the cells. The peculiarity of their centrosome apparatus aids in the differentiation from other cells. During the entire inflammatory process the emigration of polyblasts from the vessels continues, but in the later stages of inflammation, when plasma cells begin to appear, the polyblast assumes not the form of the phagocyte but of the plasma cell, and the author believes that this cell is only a form of the polyblast. Giant cells arise from a confluence of polyblasts. After the function of the polyblast is fulfilled, by far the greater number degenerate, and only a small percentage remains as plasma cells or the mixed lymphoid cells of connective tissue.—W. T. L.

Gonorrhœal Endocarditis, with Cultivation of the Specific Organism from the Blood during Life.—Harris and Johnston (*Johns Hopkins Hospital Bulletin*, 1902, vol. xiii. p. 236). The authors report a case of gonorrhœal endocarditis, in which the organism was cultivated from the blood twenty-four hours before death. The patient's fatal illness developed ten weeks after his primary urethral infection, and began with chills, headache, and prostration. During the attack of acute urethritis typical gonococci were found in the urethral discharge. His latter illness was characterized by rigor and an irregular fever. A loud systolic murmur was heard at the apex of the heart. Cultures were made from the blood on five different days. In the last one typical gonococci were obtained on hydrocele agar and in a medium consisting of a mixture of 10 c.c. of agar and $\frac{2}{5}$ c.c. of blood. At autopsy an acute endocarditis was found affecting the mitral valve, and from the enormous vegetation, as well as from the heart's blood, gonococci were cultivated. The authors review the technique of blood cultures, and conclude that except when dealing with the typhoid or paracolon bacillus a liberal dilution of blood is not necessary, and may even be fatal for the cultivation of the gonococcus where the best results are obtained when the blood is immediately mixed with melted agar and plated. Fluid media appears less satisfactory, for if it is used the oxygen supply is restricted. They conclude, further, that the bactericidal power of the blood has little

effect upon the gonococcus as compared with its action upon the typhoid bacillus.—W. T. L.

A House Epidemic of a Fever Simulating Typhoid, Caused by an Atypical Colon Bacillus, and Traced to the Water Supply.—Sion and Negel (*Cent. f. Bakt. u. Par.*, 1902, vol. xxxii. pp. 481, 581 and 679). The authors describe a small epidemic of a disease simulating typhoid fever, confined to a single household and affecting six individuals, one of whom died. The symptoms characterizing the disease were in every instance practically those of typhoid fever, and in the fatal case, what appeared as a severe attack of typhoid fever terminated with definite signs of meningitis, symptoms of this complication arising some days before death. At autopsy, seven hours after death, embolic softenings were found in the left cerebral hemisphere, with an acute, diffuse meningo-encephalitis. Endocardial vegetations were present at the apex of the left ventricle. The spleen was enlarged, the pulp friable, and both this organ and the kidneys showed anæmic infarctions. There was not a trace of swelling or ulceration of Peyer's patches, nor the least prominence or injection of the lymphatic apparatus of the intestines. The mesenteric glands were small and pale. The anatomical picture immediately suggested a severe streptococcus or pneumococcus infection; but in cultures from the gray matter of the brain, blood, cardiac vegetations, pericardium, pleural fluid, liver, spleen, and adrenals, there developed numerous colonies of a small, actively mobile bacillus, which did not stain by Gram. No other bacteria were recovered from the above situations. From four of the other patients the same bacillus was obtained in blood cultures. This organism differed from the typhoid bacillus mainly in forming gas with glucose media and in failing to agglutinate with typhoid sera; and from the colon bacillus in the absence of gas formation with lactose and the production of alkali after some days' growth in certain media. The serum from all six cases agglutinated typhoid bacilli in low dilutions and the organisms isolated from the patients in both low and high dilutions. The origin of the infection was traced to a well which was contaminated by the drainage from a neighboring barnyard. The water of this well was used by the family for drinking purposes. Cultures from the well water gave great numbers of colonies of the specific bacillus. The authors consider that their organism corresponds closely to the "paratyphoid bacilli" described by Schottmüller and isolated by him from several cases simulating typhoid fever. They believe, however, that the bacillus which they describe is more closely allied to bacillus coli than to bacillus typhosis.—W. T. L.

The Question of Fat Absorption in the Intestinal Canal and the Transport of Fat to Other Organs.—Kischensky (*Beiträge z. Path. Anat. u. Alleg. Path.*, 1902, Band xxxii., Heft 2, p. 197) says that two main theories are held by various observers as to the absorption of fat in the intestinal canal. Of these the oldest is the emulsion theory, which holds that fat is received by the epithelial cells in the form of small particles; the second theory is that fat is converted into a soluble substance by ferments or enzymes, and absorbed by the cells as such, being converted again into fat

within the cells. The author studied microscopically the intestines of young cats fed on milk or fatty acids, and sections were made through the intestines during the different periods of the absorption process. The tissues were fixed with formalin *in situ*, and a new dye, "scarlet R," having certain advantages over osmic acid and Sudan III, was used as a staining agent. In four out of twelve young cats minute fat granules were found in the peripheral zone of the epithelial cells covering the intestinal villi, but since the intestinal contents contained almost none of these extremely fine granules, the author believes that little of the fat actually enters the cells in its original state or as an emulsion. The majority of it is absorbed as a soluble material, for in striking contrast to the periphery large numbers of fat granules were found in the central portion of the cells. In young cats fat also occurred between the epithelial cells. From the epithelial cells the fat granules could be traced into the adenoid tissue of the villi, where they appeared to lie in small intracellular channels, and then could be followed through these into the lymphatics, and here they were numerous in the lining endothelial cells as well as free in the lumen. The course was then through the mesenteric lymphatics into the mesenteric lymph glands. The endothelial cells lining the lymph spaces of the glands were often packed with fat granules, and the same was true of the large cells lying free in the spaces. Fat droplets could occasionally be seen in the endothelium of capillaries in the villi; but this was exceptional, suggesting, however, that fat may enter the blood directly. Fat granules were present in the liver, kidneys, lungs, and sometimes in the spleen; frequently in the epithelium of Lieberkühn's, and Brünner's glands, and in the epithelium of the bile ducts and pancreatic ducts. Great numbers of fuchsinophilic cells were present in the walls of the stomach and intestine, and in the mesenteric glands, spleen, and lung. They rarely, if ever, contained fat. Their presence is not explained.—W. T. L.

The Presence of Elastic Tissue in Carcinoma of the Stomach.—Tsutomu Inouye (*Virchow's Arch.*, 1902, Band clxix., Heft 2, p. 278) says that twenty cases of carcinoma of the stomach were examined in order to determine what changes take place in the elastic fibres of the stomach wall during the invasion of new-growths. Sections through the normal stomach wall showed elastic fibres in great abundance throughout the submucosa and fairly plentiful in the muscularis mucosa, but very sparsely scattered through the mucosa. When sections of the stomach, which was the seat of a new-growth, were examined the earliest change noted in the arrangement of the elastic tissue was a displacement and bulging of the fibres in the muscularis mucosa, produced by the advancing growth of the tumor. As the tumor infiltrated the submucosa the fibres appeared as if broken or twisted, and were often entirely destroyed. In still older growths, when there was formation of new connective tissue, a development of young elastic fibres was also seen, not, however, in the new fibrous tissue, but about the bloodvessels. Where the bloodvessels were numerous there also was an abundance of elastic tissue, and in portions of the growth poorly supplied by bloodvessels elastic fibres were likewise few in number. Thus the origin of the new elastic tissue could be traced directly to the bloodvessels, and it was

found that they arose as delicate fibrils extending into the surrounding tissue from the old, coarse fibres of the adventitial coat. The author believes, therefore, that these new elastic fibres found in carcinomata of the stomach take their origin from the pre-existing elastic tissue of the walls of the bloodvessels.—W. T. L.

Contribution to the Cytological Study of Tuberculous Pleurisies.—BARJON and CADE (*Arch. Gén. de Méd.*, August, 1902, p. 160). The authors report in detail a study of the types of cells found in the exudates from forty-three cases of tuberculous pleurisy. Of this number twenty-five were proven to be of tuberculous origin from autopsies, sero-diagnosis, or inoculation, while the remaining observations were made from cases probably tuberculous in origin, but without definite proof of it. In practically all the cases the predominant cell was the small lymphocyte, sometimes reaching as high as 65 per cent. to 98 per cent. of the total number of cells. Early in the disease polymorphonuclear leucocytes may be present even in large numbers, but as the process develops these cells almost entirely disappear. Ravant has found a constant small percentage of polymorphonuclear leucocytes, this being true even for the early stages of the disease. The authors account for their somewhat different results by the fact that their observations were made upon centrifugalized fluid, whereas Ravant defibrinated the exudate, and thus lost sight of many polymorphonuclear leucocytes which were caught in the fibrin clots. Barjon and Cade lay little stress upon the numbers of endothelial cells present in the exudate. They believe a high percentage of small lymphocytes in the pleural exudate is a constant occurrence in tuberculous pleurisy.—W. T. L.

HYGIENE AND PUBLIC HEALTH.

UNDER THE CHARGE OF

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The Cause of Beriberi.—In a "Discussion on Beriberi" (*British Medical Journal*, September 20, 1902, p. 830) PATRICK MANSON calls attention, first, to the importance of coming to an agreement as to the meaning of the term, which, he asserts, has been applied to a variety of other diseases. He believes that even the most experienced practitioners include several distinct forms of neuritis under the one term, and he holds up the history of malaria as a warning, calling attention to the fact that, before the cause of malaria was determined, many types of non-malarial fever were regarded as malarial. Beriberi being a multiple peripheral neuritis, and this condition being the consequence of a number of causes (arsenic, alcohol,

ptomaines, etc.), it is not strange that where beriberi exists some confusion must occur. For his belief that beriberi is not arsenical neuritis, he gives a number of reasons, among which is the fact that tobacco, to which arsenic is intentionally added to give it a desired flavor, is not used in institutions, such as jails and schools, in which the disease is prevalent; and, moreover, in the treatment of the disease, arsenic is not uncommonly exhibited and causes no aggravation of the symptoms, which would occur if arsenic were the cause. Furthermore, the skin affections common in arsenical neuritis are not observed in beriberi. He holds that the great majority of cases of so-called malarial neuritis are in reality beriberi, and that the true malarial neuritis is very rare and never epidemic. He believes that beriberi is due to a toxin produced by a germ operating in some culture medium located outside the human body, and that the toxin enters the body neither in food nor in water, but through the skin or lungs. In support of his contention that the cause cannot be a germ living and multiplying in the body, he cites the fact that the most important measure in the treatment of the disease is removal of the patient from the place in which he sickened, which, if accomplished early, and provided the dose has not been overwhelming, is almost invariably followed by recovery. In proof of this statement, the details of a most interesting outbreak are given. The fact that the disease can be introduced into and spread in virgin country is given as proof that its cause is produced by a living germ. It was introduced by the Japanese into the Fiji Islands, by the Annamites into New Caledonia, and by others elsewhere. Thus far all trustworthy investigations have failed to demonstrate the presence of the germ within the human body. That the toxin does not enter the system in food he concluded long ago, by the process of exclusion and on epidemiological grounds. He has no sympathy with the rice theory, and brings forward cogent arguments against it. Proofs that the toxin is not conveyed in drinking water are too numerous to need mention, for it often happens that of two institutions side by side, supplied with the same water, one is the seat of the disease and the other is free from it. He concludes that since the disease is not caused by a germ operating directly in the human body, it cannot be passed as an infection directly from person to person; that being the result of a toxin generated by a germ outside the human body and not conveyed in food or water, it must be conveyed either by the air or through the skin, by contact or by means of some insect which inserts it under the skin, or by a combination of some of these ways; and that, unfortunately, we have nothing to show what the toxin is, nor what the germ is that produces it, nor how it gains access to the body.

Captain E. R. Rost disagrees most decidedly with Manson, and believes strongly in the alimentary origin of the disease. He relates that during an outbreak in a jail he observed that pigeons which lived in large numbers under the roofs of the jail buildings were affected by an epidemic disease, characterized by paralysis of the wings, which he attributed to a micrococcus which he found in the rice. Later, in Rangoon, he found in rice-water liquor and in mouldy rice a spore-bearing organism which was extremely resistant to high temperatures, exposure to 220° F. for nine hours being required to kill the spores. He found the same organism in the blood and in the cerebro-spinal fluid of a large number of beriberi victims. Cultures

injected into fowls caused death, and the organism was found in the blood and cord. An exactly similar disease was produced in fowls by feeding them on fermented rice obtained in the rice-liquor shops and on mouldy rice from the lower bags of damp godowns, by intraperitoneal injection of rice-water liquor, by subcutaneous or intraperitoneal injection of the venous blood of beriberi patients, and by re-injection from fowls suffering from the condition produced. The blood of beriberi patients used in the same way in pigeons produced symptoms in from one to three weeks, followed by death. Of 390 patients treated for beriberi in one institution in one year, all were adults and but few were women, and Rost believes the disease to have been due to a liquor made from damaged rice according to a process which he describes. As some outbreaks cannot be traced to the use of rice liquor or to diseased rice, he deems it probable that rice is not the only cereal in which the cause of the disease can grow, and he believes, moreover, that it is possible for the disease to be communicated through fowls suffering therefrom.

Dr. L. W. Sambon supports the rice theory, and points out the fallacies in certain observations which have been brought forward to disprove it. He believes that rice may be related to beriberi as the vehicle and not the cause of the infection. Paddy keeps sound for years, but the hulled rice is soon damaged by vegetable parasites. He cites Eijkman's statistics applying to 280,000 prisoners in Java, where one convict in thirty-nine fed on white rice has the disease, while but one in 10,000 fed on red rice acquires it. He believes that the specific agent may remain latent for a long time in the system, and thus accounts for the numerous outbreaks at sea and among people who have gone where the disease did not previously exist, and for the limitation of the infection to those who have introduced it. Infection does not spread in hospitals to other patients, and it does not attack nurses or attendants. Yet the disease is essentially a disease of collective buildings (institutions), a fact which, at first sight, might suggest contagion. Overcrowding may not be looked upon as a leading cause, for change in this regard appears to bring about no improvement. The disease breaks out just as often in new as in old buildings, and in modern battleships as well as in old wooden merchantmen.

Ronald Ross brings forward additional evidence in support of the claim that arsenic is connected with the disease. He had already published the results of analysis of the hair of twenty-two patients with the disease, arsenic having been found in traces in that of seven, principally the most recent cases. The cases which yielded negative results were, with two exceptions, of from one month to two years' duration. He records, now, the analysis of samples from eight new cases, the three most recent of which yielded positive results. The negative cases were all of more than thirty-two days' duration.

Distribution of Sewage Bacteria in Drinking Water. — Concerning the alleged ubiquity of the colon bacillus and the importance of streptococci as indicators of the presence of sewage matters in drinking water, a valuable and instructive paper is contributed by C.-E. A. Winslow and Miss M. P. Hunnewell (*Journal of Medical Research*, December, 1902),

who made bacteriological examinations of one hundred and fifty-seven samples of water from apparently unpolluted sources, and of fifty from obviously polluted sources, paying special attention to what appears to be the most important point in connection with the sanitary significance of the results of such examinations, namely, the approximate number of the organisms found. The samples were collected in 100-c.c. sterilized bottles, and in every case reached the laboratory within three or four hours. Only those organisms which gave the following reactions were regarded as colon bacilli: Fermentation of dextrose broth with production of gas in twenty-four hours; fermentation of lactose in the litmus-lactose-agar plate, with distinct reddening in twenty-four hours; production in twenty-four hours of sufficient acid in milk to cause coagulation on heating; production of nitrites from nitrates in twenty-four hours; production of indol in peptone solution in three days (all the above at 37° C.); and formation of the typical gelatin stab-growth of B. coli without liquefaction of the gelatin in seven days. Some of the organisms which resembled the colon bacillus, except in one or two characteristics, usually the power to reduce nitrates or to form indol, were classed as paracolon organisms—true colon bacilli which have lost certain functions by sojourn in an unfavorable environment. Certain organisms which produced acid, but no gas, in the dextrose tube; which coagulated milk; which failed to form indol or to reduce nitrates; and which grew best under anaërobic conditions and but feebly in media not containing sugar, were examined sometimes in more detail and were found to belong to the group of streptococci and staphylococci, regarded by Houston as characteristic of sewage. The authors conclude, as to methods of analysis, that the use of large samples in applying the colon test to the sanitary analysis of drinking water is not advantageous, for waters of good quality are more likely to be condemned, and, on the other hand, the loss of a considerable proportion of colon bacilli during incubation of large samples may cause bad waters to appear to better advantage. They suggest, also, a number of modifications in the routine process.

Single c.c. examinations of the one hundred and fifty-seven samples from apparently unpolluted sources revealed the colon bacillus but five times, the paracolon organisms also five times, and streptococci three times; but when 100 c.c. were employed, the same organisms were detected, respectively, eleven, five, and ten times. Single c.c. examinations of the fifty samples from obviously polluted sources showed the colon bacillus in thirteen, the paracolon group in six, and streptococci in twenty-five; and 100 c.c. samples yielded but four positive results as to the colon bacillus and twenty-two as to streptococci.

Infection through Droplets and Dust.—Attention is called by B. HEYMANN (*Zeitschrift für Hygiene und Infectionskrankheiten*, xxxviii. p. 21) to the fact that Koeniger, Kirstein, Hutchinson, and others, who have studied the subject of infection through droplets expelled from the air-passages through sneezing, coughing, and speaking, have not employed the bacillus of tuberculosis in their experiments, but have made use of other bacteria. In a series of experiments conducted by himself, he made use of a glass cabinet of three cubic metres' capacity, in which coughing consumptives

were confined up to one and a half hours. Dishes and plates were placed in different situations within the cabinet, for the purpose of catching the expelled droplets, and at the end of each exposure these were rinsed out and rubbed with a small amount of broth, which was then injected into the peritoneal cavity of guinea-pigs, which, after ten or twelve weeks, indicated by their condition whether or not virulent bacilli had been thrown out. He demonstrated that some individuals produce at times, not only in front but on all sides, a mist of droplets containing living germs. The majority of these droplets are large and settle quickly, but some are very small and are projected more than a metre, and remain in suspension sometimes more than an hour. These results demonstrate the importance of holding a handkerchief before the mouth while coughing. The duration of life of the bacilli within the droplets was determined as eighteen days when protected from light, and three days when exposed thereto. A second series of observations concerning the formation and movement of tuberculous dust from dried deposits on carpets, floor-boards, and handkerchiefs showed that the last-mentioned objects are more causative of danger than the others, since when they are rubbed or waved they give off a very fine dust which remains a long time in suspension, while that stirred up from the carpets and floor-boards through ordinary mechanical means is sent but a short distance into the air, and soon settles back. He concludes that dust is considerably less dangerous as a carrier of infection than droplets.

The subject of penetration of bacteria into the lungs through inhalation of droplets and dust has been investigated by Oscar Nenninger (*Ibid.*, p. 94), who found that, whereas very small numbers of bacteria are almost always present in the air-passages and lungs removed with all care from animals (sheep, swine, and rabbits) immediately after slaughter, numerous colonies of B. prodigiosus were present in all parts of the lungs of guinea-pigs and rabbits exposed for ten minutes to the spray of a culture of that organism and then immediately killed. The same result was observed when a culture was smeared on the buccal mucous membrane and the animal was forced to breathe through the mouth by closure of the nostrils. Dust containing spores of B. megatherium reached even the finest branches of the air-passages, but the number of organisms found was materially smaller than was observed when droplets were inhaled, manifestly because dust particles require greater rapidity of movement of the air for their convection, and because they are more easily caught and detained by the mucous membrane. Owing to the normal bactericidal action of the tissues, infection follows seeding with pathogenic germs only when local conditions are favorable thereto.

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A CONTRIBUTION TO THE ANATOMY AND SURGERY OF THE TEMPORAL BONE.

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The recent additions to the symptomatology and diagnosis of complications and sequelæ of middle-ear disease, with the resulting surgical interference in deep-seated affections, have made it necessary to acquire a more intimate knowledge of the landmarks of the ear and its surrounding structures. The present article, with the accompanying charts drawn from dissections on the cadaver, is intended to fill a requirement still existing in our medical literature and to serve as a guide for improved technique in the future for attacking the temporal bone and vital parts in its immediate neighborhood.

In the comparatively simple procedure of entering the mastoid antrum an incision through the skin, fascia, and periosteum, beginning behind the attachment of the auricle, at a point corresponding to the upper wall of the external auditory meatus and passing over the middle of the mastoid process to its tip, will suffice if the tissues are drawn forward to expose sufficient bone to appreciate the landmarks necessary for this operation. In the more extensive procedure of attacking the middle ear and its adjacent parts, a longer incision is necessary. The incision begins at a point above the ear sufficiently far back to avoid the temporal artery, then courses downward ½ to 1 cm. behind the attachment of the auricle, in order to avoid severing the

posterior auricular artery, and ends at the tip of the mastoid process (Fig. 1).

When the tissues are dissected and retracted a field will be exposed in which the entire outer and middle ear, as well as the mastoid antrum and the sigmoid flexure of the lateral sinus, can be reached (Fig. 2). Above the temporal ridge this incision should pass through skin alone, exposing the temporal fascia covering the temporal muscle; this should not be severed. Below the ridge it should pass directly to the bone of the mastoid process. The anterior flap should contain the auricle with the periosteum from the mastoid process and the entire soft parts of the external auditory meatus, the periosteum of the meatus remaining continuous with that covering the mastoid process. On elevating the periosteum and retracting the tissues still covering the process behind, an area will be exposed sufficient for the most radical operation on the temporal bone, even to the extent of its entire removal.

The following are the landmarks visible from above downward (Fig. 2): Above the temporal ridge or crest is the fascia covering the temporal muscle. The crest is the continuation backward of the zygomatic arch and affords attachment to the fascia as well as the temporal muscle, and corresponds in height to the upper wall of the bony auditory canal; it forms the division line between the squamous and mastoid portions of the temporal bone, and serves as a landmark for opening the mastoid antrum and lateral sinus.

In a simple mastoid operation the external opening should remain below this crest in order to avoid entering the cerebral cavity.

Below the crest and in front of the mastoid process is seen the external auditory meatus, a long, funnel-shaped canal, the walls of which are formed by the tympanic plate. The free margin of this plate (the auditory process) affords attachment to the cartilage of the ear.

In the depth of the meatus is seen the tympanic membrane or ear drum, lodged in a ring of bone with the manubrium or handle of the malleus, attached to and shining through its upper half, slanting from above and in front downward and backward. The upper portion of the membrane is thrown into folds by the outward projection of the processus brevis of the malleus, which springs from the upper part of the manubrium close to the tympanic ring. The portion of the membrane thus affected is called Shrapnell's membrane.

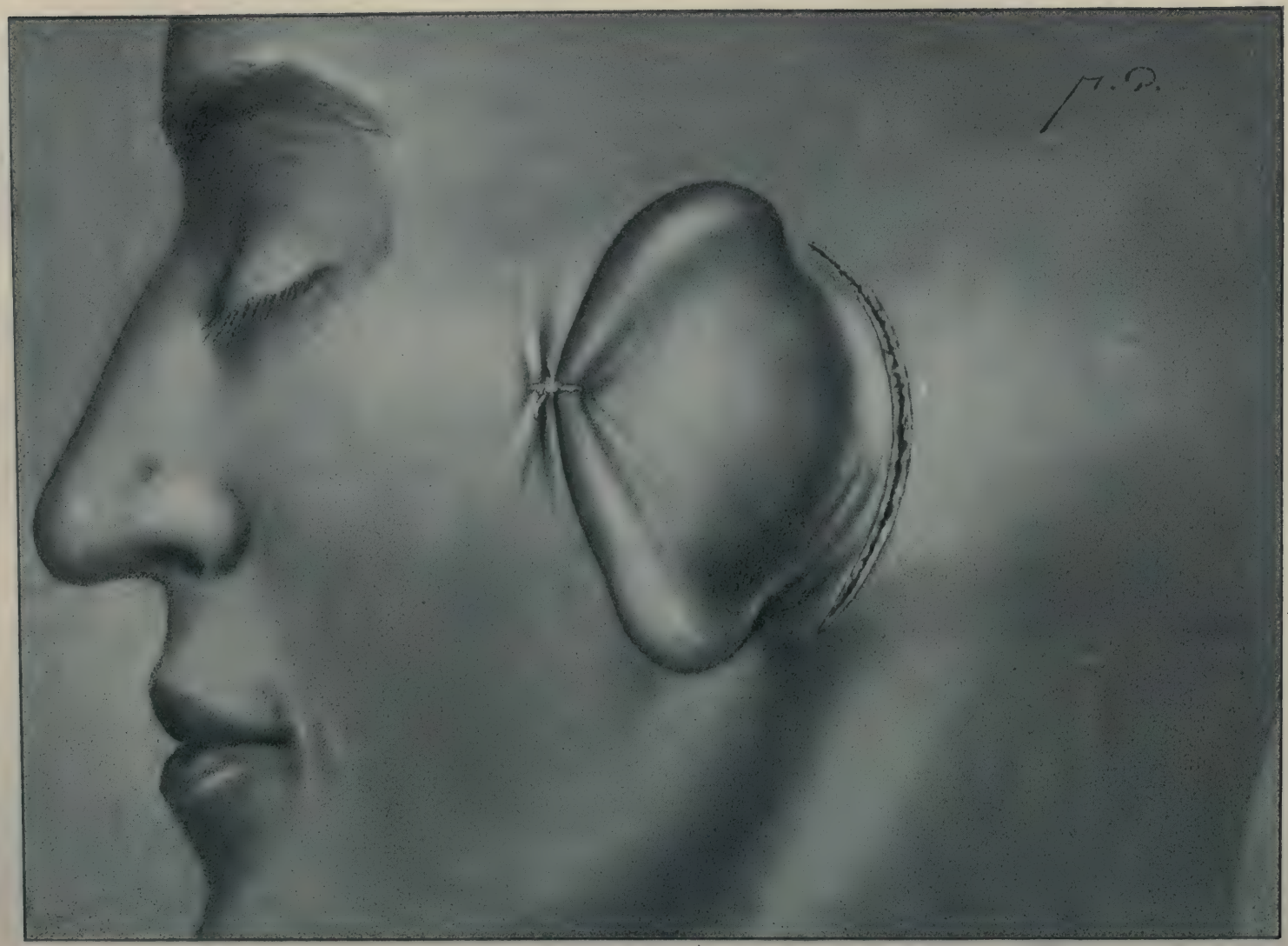
On removing the tympanic membrane from its ring of bone and from its attachment to the malleus, the tympanic cavity or middle ear is exposed and the following points of interest noted (Fig. 3): In the upper half of the cavity are seen anteriorly the manubrium, projecting downward and slightly backward, with the processus brevis at its upper end close to the rim of the bony canal. The processus longus of the incus is situated half a millimetre behind and parallel to the manu-

brium, and has its lower end attached to the stapes. The lower half of the cavity presents a rounded, glistening eminence, called the promontorium, and an opening directly behind it called the fenestrum rotundum. The latter opens into the cochlea, of which the promontorium represents the first turn.

In order to expose the tympanic cavity or middle meatus more thoroughly, a part of the superior and posterior walls of the external meatus can be removed (Fig. 4). The tympanic cavity (as seen in the last figure) has its upper part, the atticus, hidden behind the inner portion of the upper wall of the external auditory meatus. Hence, the upper wall of the meatus corresponds to the outer wall of the atticus, and with the procedure just mentioned the atticus is exposed.

The atticus contains the heads and bodies of the malleus and incus, and the removal of its outer wall shows these bones *in toto*. Besides these structures the tensor tympani muscle can be seen anteriorly emerging from its canal and becoming inserted into the neck of the malleus. The short process of the incus is seen projecting back into the aditus, while the long process descends to become attached to the stapes. Beneath the short process of the incus the chorda tympani nerve emerges from the facial canal in the posterior wall. It crosses the long process of the incus and disappears behind the malleus. When this nerve is injured accidentally or otherwise, the sense of taste for the corresponding side of the tongue is lost. Directly internal to the tip of the long process of the incus lies the stapes placed at right angles to it. To the neck of the latter is attached the stapedius muscle, which consists of minute fibres 1 to 2 mm. in length coming from the pyramidal-shaped cavity in the posterior wall of the middle meatus. In the background, portions of the inner wall of the middle ear are visible. Directly above the stapes and behind the incus is the projection of bone covering the facial nerve. Below the stapes, the promontorium and fenestrum rotundum are again seen as before.

At the upper posterior angle of the entrance to the bony meatus is a spicule of bone known as the suprameatic spine (Figs. 2 to 5). This is of importance in the simple mastoid operation, as it is prominent in most skulls, and when felt, serves as a landmark, being the most anterior point to which the tissues should be dissected, and also the point 1 cm. behind which the opening for entering the atrium should be begun. The mastoid process, of which the temporal ridge forms the base line, has been denuded of periosteum. Near its posterior border is situated the mastoid foramen, through which one of the emissary veins of the lateral sinus passes. Below, the process has the sternocleidomastoid muscle attached to it. The fibres of this should be left intact when these parts are exposed, excepting in those instances in which their presence interferes with the thorough exploration of the mastoid cells.



The nature of the bony structure of the process varies greatly in different subjects, being very compact tissue (small celled or diploic) in some and cellular (large celled or pneumatic) in others.

To reach the antrum, the chisel or burr drill must be placed at a point 1 cm. behind the suprameatic spine, and keeping below the temporal crest, or the upper wall of the meatus, must penetrate a mass of bony tissue to a depth varying from 1 cm. to 2 cm. in a direction inward, forward, and slightly upward, corresponding to the direction of the external auditory canal. The position of the antrum varies somewhat. Although it is generally situated about ½ to 1 cm. behind the outer opening of the auditory canal, it is sometimes found almost directly internal to its upper wall. The depth at which the antrum is met also varies, but it is safe to say that if the instrument penetrates deeper than 1½ cm., and be directed too far forward or downward, the horizontal semicircular canal or the aqueductus Fallopii will be encountered (Fig. 7). If the former were opened in a purulent otitis media the pus would travel along it to the vestibule and from there into the internal auditory meatus, producing a pachymeningitis or extradural (epidural) abscess of the posterior fossa of the skull; or from the vestibule through the perpendicular semicircular canal, which if accompanied by erosion of its bony covering would lead to involvement of the meninges of the middle fossa. The same would hold good for the posterior semicircular canal affecting the posterior fossa.

If the latter (the aqueductus Fallopii) were opened an inflammation of the facial nerve which is contained therein would result, producing paralysis of that side of the face. The inflammatory process might also find its way through the entire canal to the internal auditory meatus, causing a pachymeningitis or extradural abscess as mentioned above; or, travelling along the nerve to its cerebral attachment, would produce a meningitis or subdural (intradural) abscess. The direction of the penetrating instrument must also be forward, in order to avoid injuring the lateral sinus.

For extensive dissections on the mastoid process, where involvement of the antrum as well as the lateral sinus and the mastoid cells is suspected, a division of the process into four equal parts suggested itself to Dr. Hartley, and the following procedure has been evolved[1] (Figs. 3, 4, and 5): The temporal ridge, or a line continuous with the zygomatic arch, is taken as the upper boundary; the anterior border of

[1] In Chipault's "Surgery" reference is made of the division of the mastoid process for the purpose of locating the lateral sinus.

EXPLANATION OF FIG. 1.

Line of incision for radical operations. × Point from which incision for "mastoid operation" is made.



the mastoid process, as the anterior boundary; a line drawn vertically from the junction of the posterior border of the mastoid process where it meets the occiput, as the posterior boundary; and an imaginary line drawn backward from the tip of the mastoid process, as the lower boundary of a quadrangle. On dividing this into four equal parts it was found that in almost every instance the upper anterior quadrant opened into the mastoid antrum, the upper posterior quadrant opened into the lateral sinus, and the two lower quadrants into mastoid cells. The lower posterior quadrant also opens into the descending limb of the lateral sinus if gone into sufficiently deep.

In permitting a wall of bone to remain separating the anterior and posterior quadrants, a safeguard is established which prevents the infectious discharge which might be found in the anterior quadrant (antrum), entering and setting up a similar process in the posterior quadrant with its lateral sinus, providing this has been exposed and found to be healthy and patent.

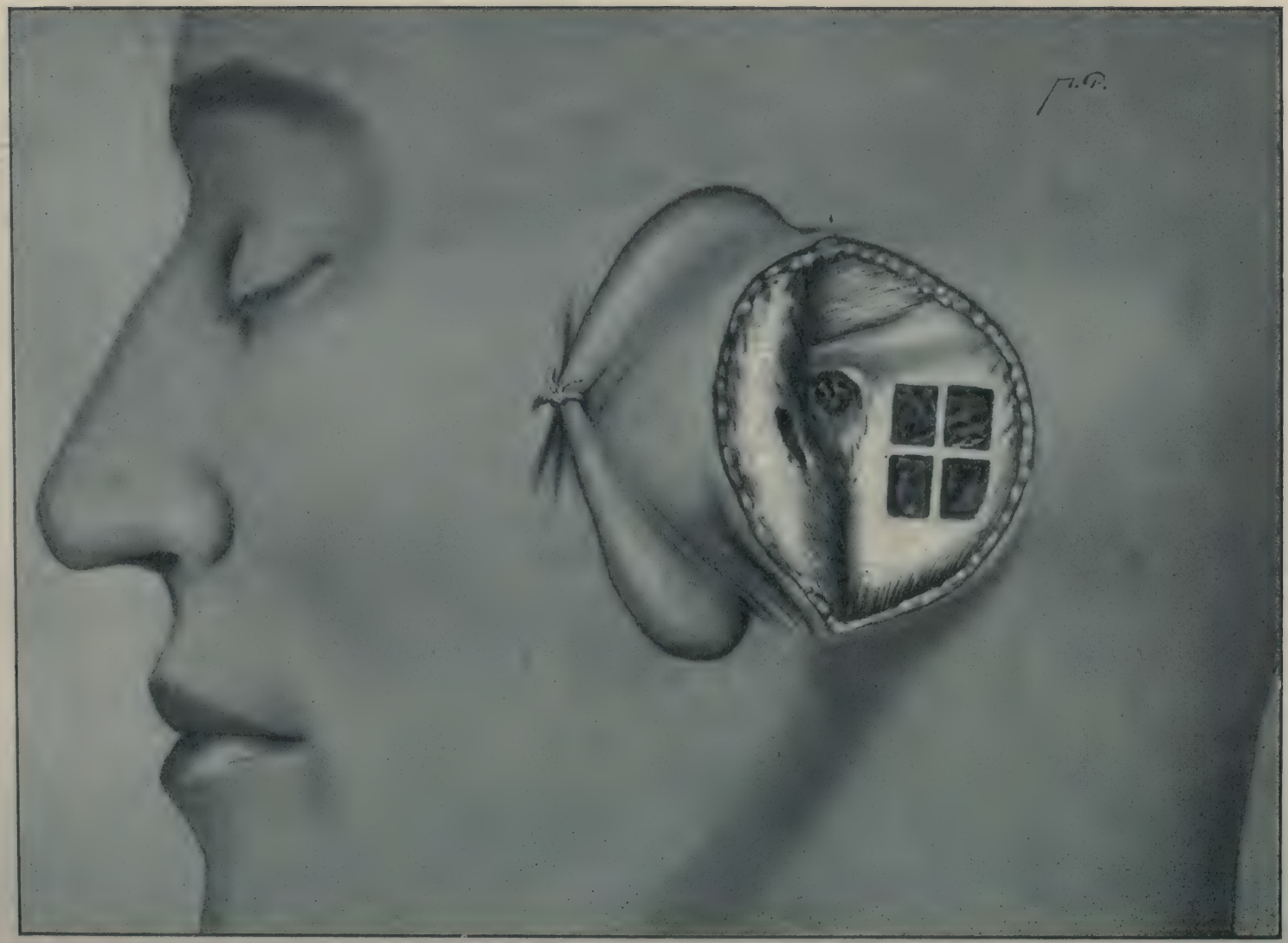
In this way, if any doubt exists as to the extent of infection, the entire surface of the mastoid can be immediately mapped out, and the upper anterior quadrant opened first to determine if the antrum is involved (Fig. 4). If this be so and the mastoid cells themselves contain pus, one or both lower quadrants can be opened and evacuated. If the process is very extensive, and there is reason to suspect an infected thrombus in the descending limb of the sigmoid flexure of the lateral sinus, which is the most frequent site for a beginning thrombus, the upper posterior quadrant can be gone into, the sinus punctured with a hypodermic needle or incised, if sufficiently exposed, and the nature of its contents determined. The bridges of bone between the quadrants have the advantage over a continuous bony wound, made by chiselling off the entire outer surface of the mastoid, as performed by many surgeons, on account of the support given the tissues which preserve the original contour of the parts, and the barriers which they form between infected and non-infected areas.

The descending limb of the lateral sinus is met at a depth ranging from ½ to 1 cm., and is usually seen taking a somewhat slanting course from above and behind, down and forward; it then dips in forming the sigmoid flexure. The sinus generally fills the upper posterior quadrant, but at times it will be seen only in the posterior half or two-thirds of the quadrant, and in these cases the quadrant can be enlarged posteriorly. Frequently the mastoid vein can be seen

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EXPLANATION OF FIG. 2.

Tissues exposed with incision as indicated on Fig. 1, showing tympanic membrane with manubrium of malleus, tympanic plates with auricular process, and suprameatic spine. Behind the meatus the temporal fascia, temporal ridge, mastoid process, mastoid foramen and sternocleidomastoid muscle.



entering the sinus at this point (Fig. 4). This vein is of importance in case of periostitis of the mastoid process, as the inflammation of its walls and its extension inward may be the origin of a thrombus of the lateral sinus; and in cases where the thrombus of the sinus already exists, the blood which is dammed up in the mastoid vein produces œdema of the tissues which it drains, and becomes of diagnostic importance in determining the former condition.

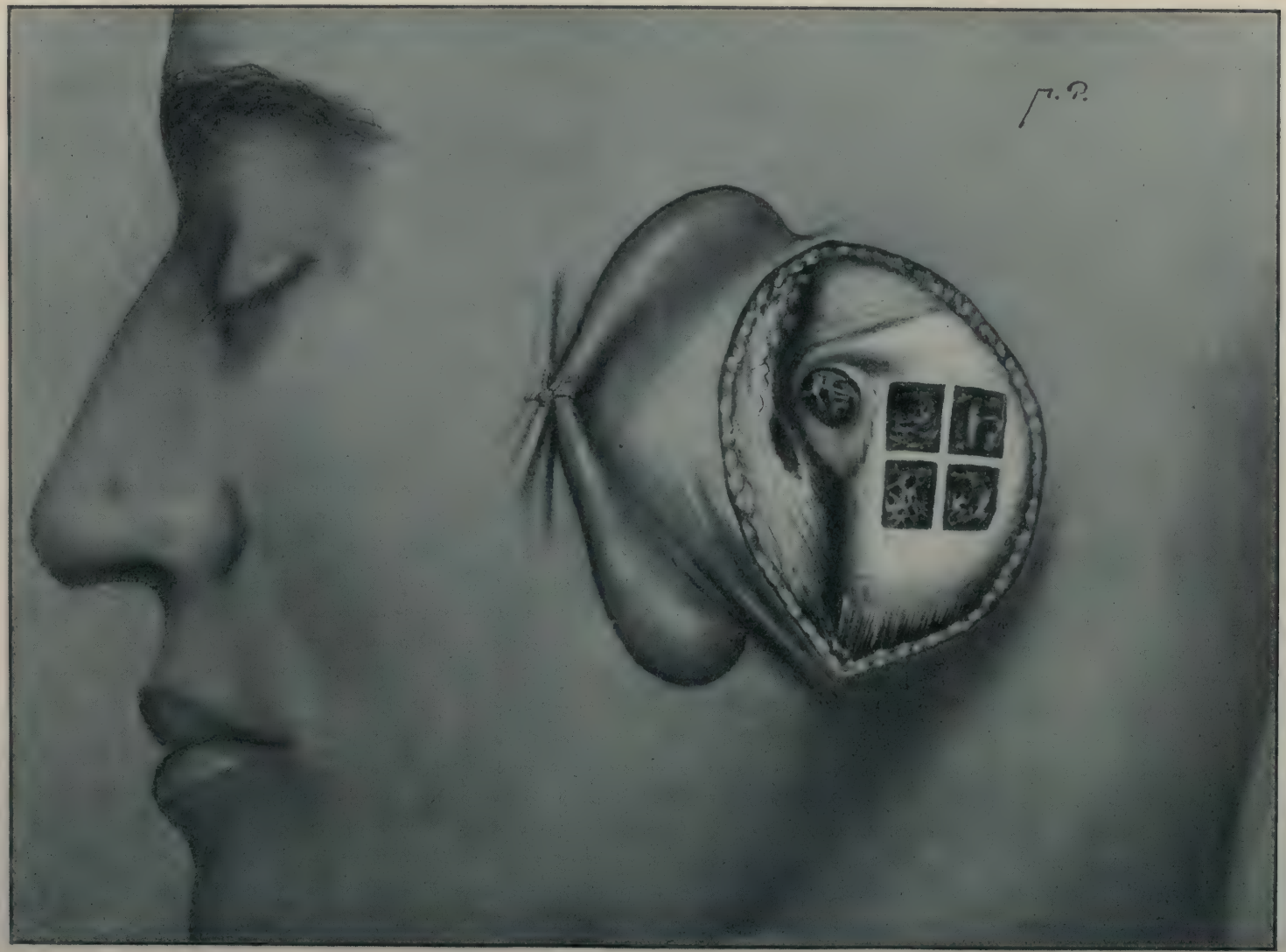
On returning to the description of the middle meatus we find that by severing the tensor tympani muscle in front, and the articular attachment of the incus below, both the malleus and incus can be removed, leaving the stapes *in situ* (Fig. 5). On removal of these two ossicles, the entire inner wall of the meatus can be seen. The upper part, which also forms the inner wall of the atticus, consists of a rounded projection, formed by the horizontal semicircular canal above and a lighter strip below, made up of a thinner plate of bone covering the facial nerve and forming the aqueductus Fallopii. The aqueductus Fallopii extends farther forward than the semicircular canal to the anterior and uppermost angle of the meatus. Below this projection the stapes is seen lodged in the fenestrum ovale, with the stapedius muscle, coming from behind, inserted into its neck. The promontory and fenestrum rotundum forming the lower half of the inner wall are seen to better advantage. The chorda tympani nerve has been removed.

To effect a more thorough and immediate exposure of the entire middle meatus, when radical measures are intended, the removal with a chisel of the tympanic plate as far as the styloid process, in combination with the removal of part of the upper and posterior walls of the external auditory canal, will be found of the greatest advantage as a preliminary step (Fig. 6). By removal of this plate of bone and the superficial lamina of the anterior surface of the mastoid process the entire facial nerve can be exposed and located and followed to the bend in the nerve at the upper anterior angle of the middle meatus. The nerve is lodged at a depth of 2 cm. from the external surface of the mastoid process. Hence, no fear need be entertained of its injury in this part, as it is rarely necessary to penetrate the process to that extent in mastoiditis. But the importance of the anatomical relation of the upper part of the facial nerve (as shown in Figs. 4 and 7) cannot be too strongly emphasized, as its position is such and its protection so slight that in simple operations on the drum or on the contents of the middle ear, or the faulty direction of the chisel in opening the mastoid antrum, the canal may be opened and the nerve injured (abraded,

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EXPLANATION OF FIG. 3.

Exposure of middle meatus after removal of tympanic membrane, showing manubrium of malleus, processus longus of incus, promontorium, and fenestrum rotundum. Also pneumatic cells in "mastoid quadrants."



crushed, incised, or severed), thus producing most disagreeable after-effects. The stapes is seen once more lodged in the fenestrum ovale directly below the course of the nerve, but devoid of its muscle on account of removal of its casing of bone posteriorly.

The aditus and antrum (indicated by arrow in Fig. 6) or passage leading from the upper part (atticus) of the middle meatus to the antrum, along which the infection of a middle ear disease so often travels into the antrum, can be shown by removing a sufficient amount of bone from the upper and posterior walls of the bony meatus (Fig. 7). (This is one of the steps in the Stacke-Schwartze "radical operations.") When this is done the plate of bone forming the roof of the tympanic cavity (called the tegmen tympani) is seen; that portion of bone forming the roof of the antrum is called tegmen antri. The tegmen is very thin (½ to 2 mm.) in most skulls and at times incomplete, and can easily be eroded by the acrid discharge of a middle ear disease. This complication often leads to the formation of an extradural abscess of the middle fossa of the skull or to inflammation of its dural lining, which in time may lead to intradural or cerebral abscesses or to inflammation of the entire arachnoid or pia mater.

With the exposure as described, all the necrosed or diseased bone can be removed, which in itself is often sufficient to check an inflammation of the meninges or brain which has been caused by the necrosis.

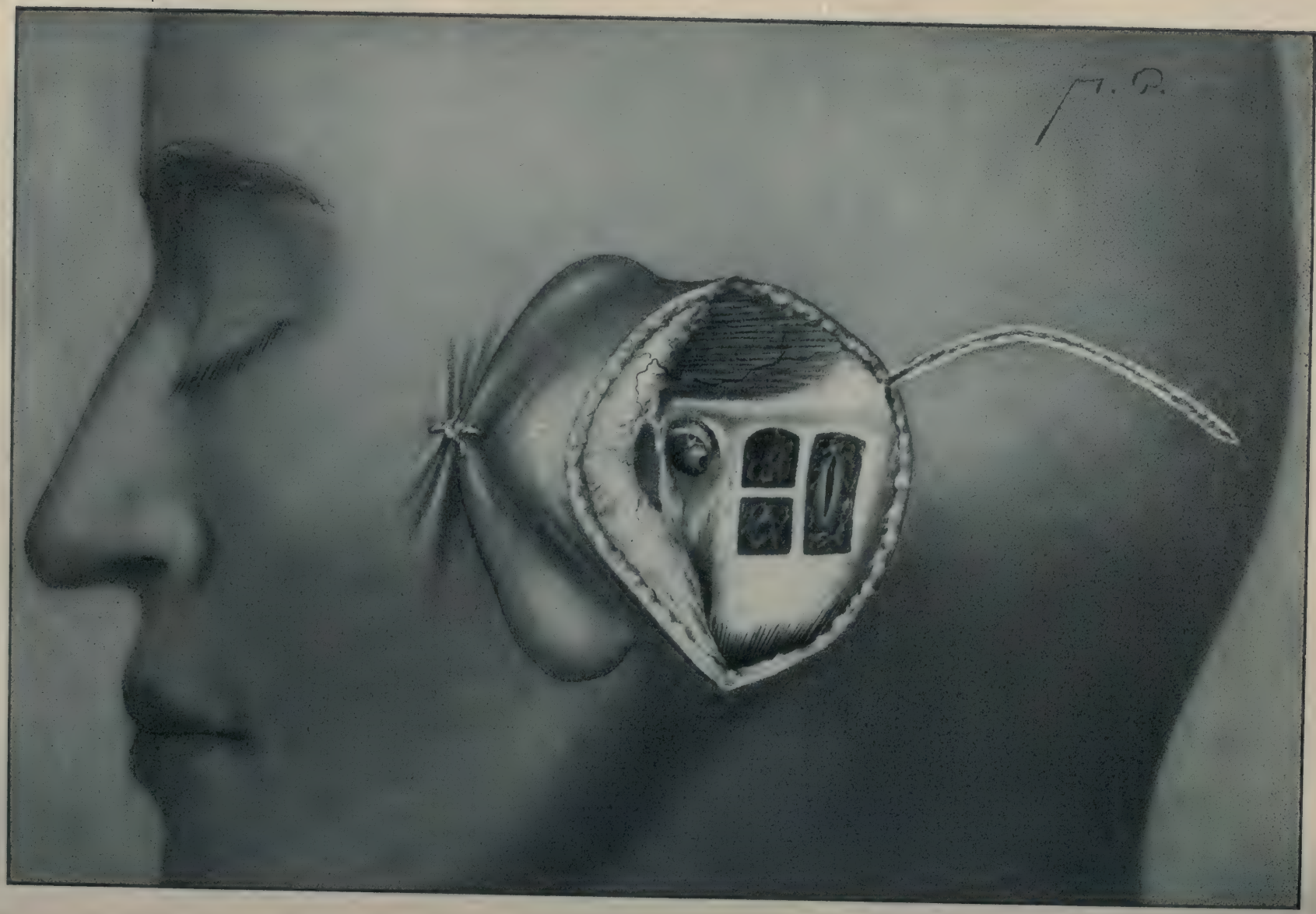
An extradural abscess can be drained through the opening made in the tegmen, while a deep-seated one could be more easily reached through the opening in the squamous plate, as will be mentioned farther on (Figs. 6 and 7).

On removal of the outer wall of the aditus, as mentioned, the projection formed by the horizontal semicircular canal is seen forming a part of the floor and inner wall of the aditus (Fig. 7). It will be readily understood how easily the canal can be opened if on exposing the antrum the chisel is directed too far forward or downward at a depth greater than 1½ cm.

On dislodging the facial nerve from its groove, the inner wall of the aqueductus Fallopii is shown extending from the upper anterior angle of the middle meatus backward directly below the horizontal semicircular canal, with the fenestrum ovale beneath it; it then bends downward, with the fenestrum rotundum in front of it, and reaches the stylomastoid foramen at a depth of about 1½ cm. from the outer surface of the mastoid process.

EXPLANATION OF FIG. 4.

Portion of upper and posterior walls of external bony meatus removed, showing tensor tympani muscle attached to malleus anteriorly; chorda tympani nerve emerging from aqueductus Fallopii, posteriorly, crossing incus; below this the stapedius muscle, promontorium and fenestrum rotundum. The upper anterior quadrant shows the mastoid antrum; the upper posterior, the lateral sinus with mastoid vein; the two lower quadrants, mastoid cells.



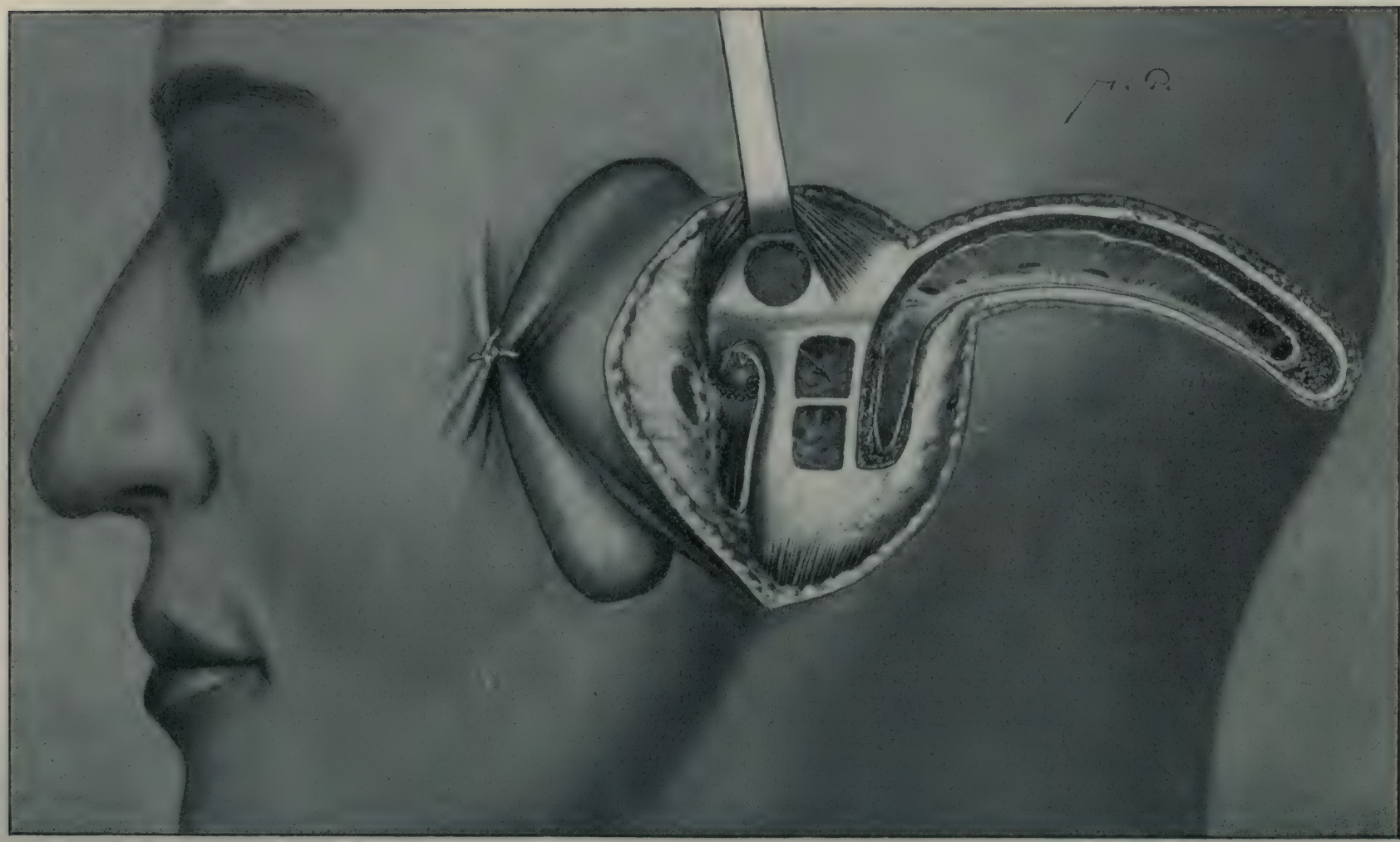
On removal of the tympanic plate the floor of the tympanic cavity is seen to consist of bone varying in thickness from ¼ to ½ cm. Frequently this helps to form the outer wall of the jugular fossa, and where necrosis of the bone or inflammation of the communicating veins in the bone has taken place, an inflammation or thrombosis of the bulbar portion of the jugular vein, which is contained in the fossa, results.

Continuing with the dissection of the mastoid process, we find that on removing the ledge between the upper and lower posterior windows (as shown in Fig. 5) and making them continuous, a longer stretch of the descending limb of the sigmoid flexure of the lateral sinus can be exposed, and its walls more readily incised, if it is necessary to inspect its interior or to determine its contents. By inspecting its interior you can determine if an adhering thrombus exists which does not clog the entire lumen. Incomplete thrombi are more frequent where the sinus enters the jugular vein in a more or less straight line, while if they join at an acute angle the thrombus is more often complete. A coating or granulations on the outer side of the sinus, or necrotic areas in its wall, make the presence of a thrombus probable. If no clot is present in such a case, the opening must be packed with gauze and equable pressure made, by means of a graduated conical compress, to control the hemorrhage. If the inner wall is to be inspected, the hemorrhage must be controlled by packing or compressing the sinus at both ends. If a clot is found, this must be removed and the ensuing hemorrhage controlled as just mentioned. If the entire removal of the clot is not successful, an extended incision must be made above or below or in both directions, according to the extension of the clot, so that complete patency of its lumen is established and the entire sinus can be inspected for possible necrosis of its wall.

The entire course of the sinus can be exposed above by an incision commencing at the upper posterior quadrant in a direction upward and backward and then gradually downward until it reaches the external occipital protuberance, which corresponds on the inside of the skull to the torcular Herophili (Fig. 5). The bone covering it can be removed by means of a chisel, circular saw, or drill, and the dural covering incised along its entire course, if this should be found necessary in order to remove the clot or infected matter filling the canal, or to excise the wall itself if found necrotic (Fig. 6).

EXPLANATION OF FIG. 5.

The malleus, incus, and chorda tympani nerve removed from middle meatus, showing projection formed by external semicircular canal and aqueductus Fallopii, stapes in fenestrum ovale with stapedius muscle attached posteriorly. Ledge removed between posterior quadrants exposing descending limb of lateral sinus (sigmoid flexure), which is incised. Incision from upper posterior quadrant backward for exposure of horizontal limb of lateral sinus.



About 1 cm. above the posterior window the slit leading to the superior petrosal sinus can be seen. Posteriorly the opening to the sinus of the other side is visible, and somewhat in front and above this the longitudinal sinus has its termination. Along the entire course of the lateral sinus, slits representing the entrance of cerebral veins can be seen. Frequently fibrous bands are also found stretching across the lumen and forming supports to maintain the patency of the canal against the pressure exerted by the weight of the brain.

Below and in front, corresponding to the lower posterior window, the sinus will be seen to dip in toward the jugular fossa, forming the lower limb of the sigmoid flexure.

If the symptoms and physical signs of the case make probable the presence of an extradural, intradural, or cerebral abscess, especially of the temporal lobe, which occurs more frequently, or the presence of fluid in the ventricles, a puncture of the brain in various directions can be made through a trephine opening in the squamous portion of the temporal bone. This can be readily exposed on retracting the temporal muscle upward after removal of its fascia (as shown in Figs. 5 and 6). On removing the button of bone, a branch of the middle meningeal artery is frequently seen traversing the space. A long aspirating needle or narrow-bladed knife can be passed into the brain in various directions until the presence or absence of pus in the brain or excessive accumulation of cerebro-spinal fluid in the ventricles is determined and located. If pus is found and the trephine opening is not of sufficient size to afford proper drainage, the temporal muscle can be still further detached and all the soft parts be retracted upward and forward so that the opening can be enlarged in various directions.

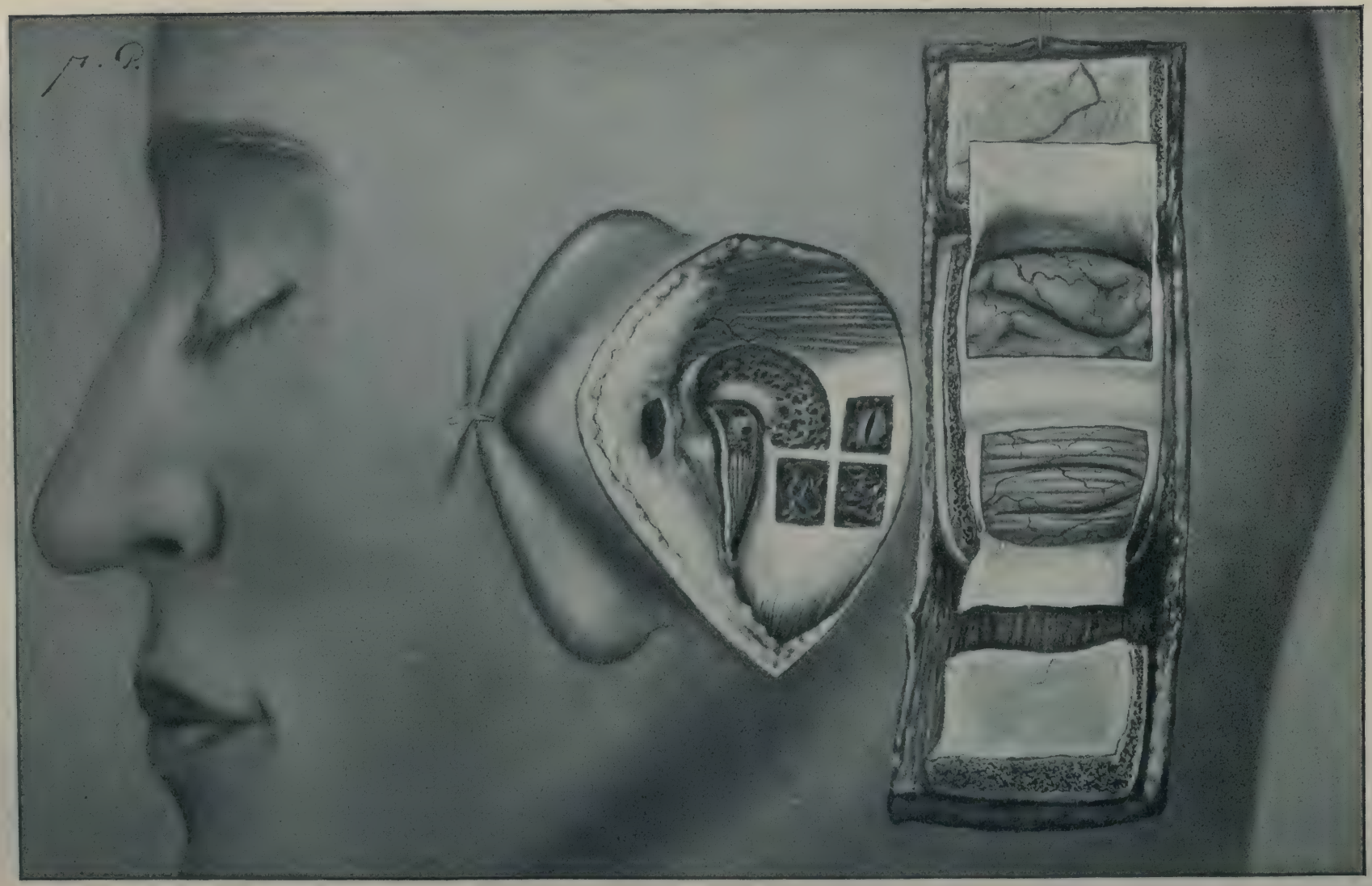
If the diagnosis of abscess is positive beforehand, and the cerebral cavity is to be opened in combination with the radical ear operation, a quadrilateral osteoplastic flap is made of the squamous portion of the temporal bone and turned forward as mentioned farther on.

If on incising the lateral sinus in the upper posterior window (as shown in Fig. 7) a suspected sinus affection is not found to exist, but the train of symptoms points to the presence of a serious complication in this region, the dura of the cerebral or cerebellar lobes can be exposed by a single or double "trap-door" incision, the course of the lateral sinus serving as a median line from which the osteoplastic flaps can be cut above and below. The incision in the dura mater

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EXPLANATION OF FIG. 6.

Outer wall of aqueductus Fallopii and the tympanic plate has been removed, exposing the facial nerve. Arrow in aditus ad antrum. Interior of entire lateral sinus exposed, showing slit for superior petrosal sinus anteriorly and openings for longitudinal and right lateral sinus posteriorly. Trephine opening in squamous plate, with middle meningeal artery showing.



should be made on three sides only, and should leave a sufficient margin to which the flap can be sewed when replaced subsequently.

Through this exposure the occipital convolutions of the cerebrum, the entire half of the tentorium cerebelli, and the posterior fossa of the skull, with its cerebellum, can be inspected, and extradural, intradural, or brain abscesses can be incised and drained. A simple and tolerably accurate method of locating the horizontal limb of the lateral sinus, without the aid of the mastoid quadrants, is Chipault's method, which consists in taking a point 95 per cent. of the distance between the nasion and inion and joining it by a straight line with the retro-orbital tubercle. The posterior half represents the course of the horizontal limb of the sinus (see sketch under technique, below).

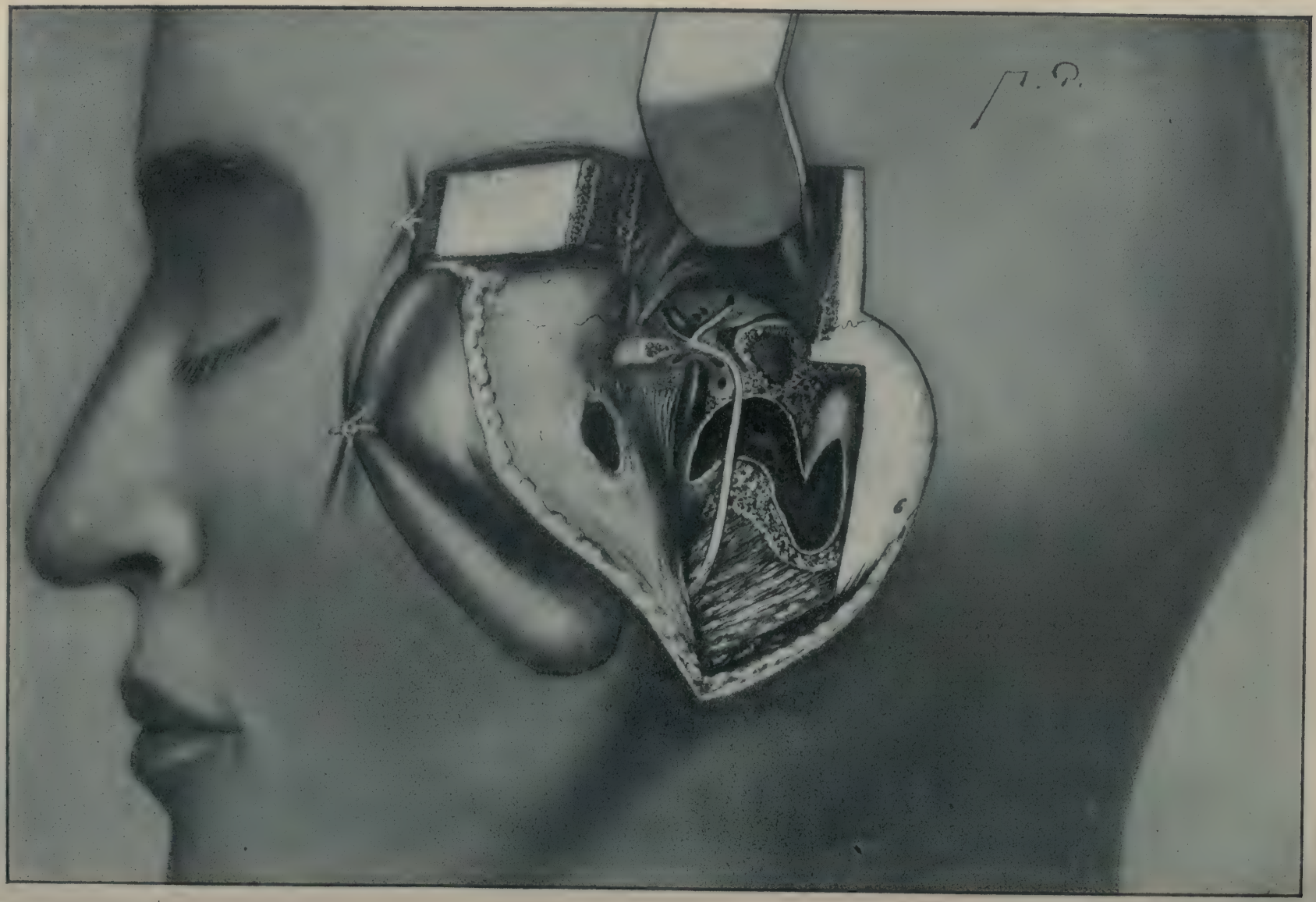
To afford a sufficient exposure for a very deep dissection of the petrous portion of the temporal bone, it is necessary to remove a plate of bone from above the ear, preferably quadrilateral in shape, about 4 cm. long and 3 cm. wide, to include the portion of the squamous plate lying over the posterior half of the zygomatic arch, and reaching back as far as the middle of the mastoid process. The flap, containing skin, muscle, and bone, and nourished by a branch of the temporal artery, is turned forward (Fig. 8).

By retracting the dura from the upper surface of the petrous bone, resistance will be met with in front, where the middle meningeal artery emerges from the foramen spinosum. At a depth of about 3 cm. from the exterior of the skull the carotid artery can be exposed on removal of its bony canal from above. The cochlea will be found situated in the angle formed by the artery as it bends inward and forward from below, while the Eustachian tube, with its gallery containing the tensor tympani muscle, hugs it anteriorly (Fig. 11). The opening of the Eustachian tube in the upper anterior angle of the middle meatus is directly in front and external to the ascending limb of the artery. In cases where but a thin layer of bone covers the artery, or where the bone is entirely absent in this situation, the artery can be seen pulsating on examining the middle ear, and its puncture by a paracentesis needle carried too deeply is possible. Here, too, necrosis of the inner wall of the tympanic cavity, forming the bony canal of the artery, can produce a destructive process in the wall of the vessel and cause fatal hemorrhage if not ligated below in time. The artery is at a depth of about 2 cm. from the auditory process, and

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EXPLANATION OF FIG. 7.

Bone of external meatus and outer wall of aditus ad antrum chiselled away, exposing the tegmen tympani, tegmen antri, atticus, aditus ad antrum, mastoid antrum, and external semicircular canal. The facial nerve is dislodged from the aqueductus Fallopii, and the fenestra ovale and rotundum appear below. Posteriorly two osteoplastic flaps, with horizontal limb of lateral sinus chosen as median line for exposing cerebral and cerebellar convolutions.



has the jugular vein directly behind it and somewhat to its outer side. In all the previous dissections the facial nerve has been exposed only from the anterior superior angle of the middle meatus. If we follow the course of the nerve in the aqueductus Fallopii as it emerges from the internal auditory meatus and passes forward between the cochlea and vestibule, it forms an angle of 45° with the long axis of the skull (Figs 8 and 11). As it enters the middle meatus it turns outward and backward, forming an elbow from the point of which the superficial petrosal nerve is given off. The latter passes inward and forward through the hiatus Fallopii along the upper surface of the petrous bone until it reaches the middle lacerated foramen.

The base of the cochlea is formed by the anterior wall of the internal auditory meatus; its apex juts against the Eustachian tube. To its inner side is the carotid canal; to its outer the aqueductus Fallopii, with the facial nerve above and the vestibule below.

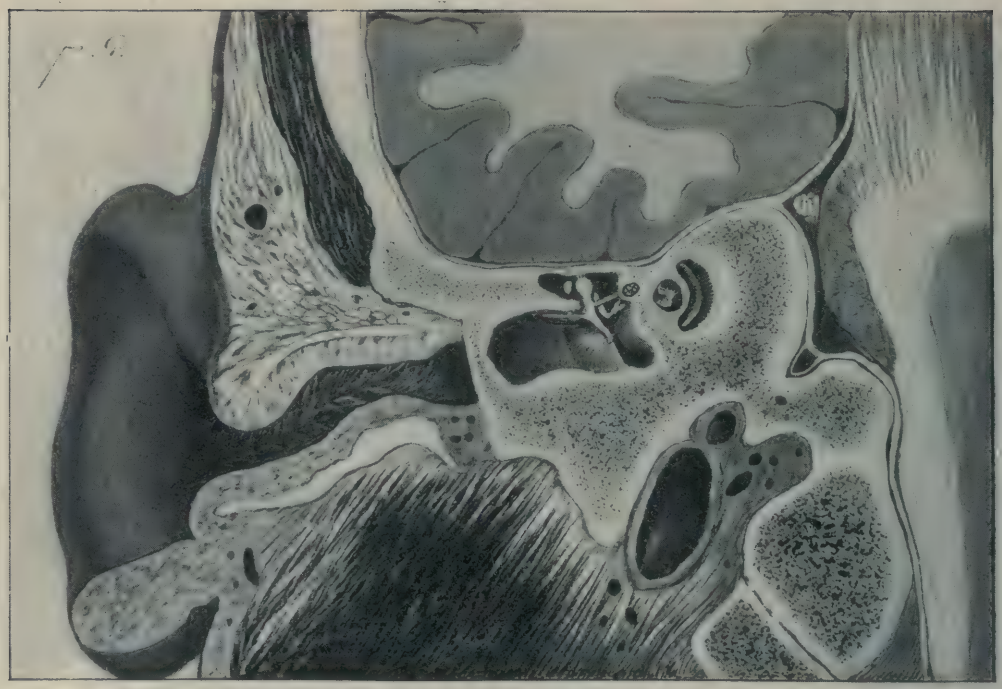
The vestibule is seen at the outer side of the facial canal with the horizontal semicircular canal coming from it externally, and the perpendicular semicircular canal superiorly.

The exposure of the sigmoid flexure of the lateral sinus has been brought about by the removal of almost the entire mastoid process (Fig. 8). In this procedure injury to the facial nerve must be avoided. This nerve emerges from the stylomastoid foramen, at the depth of about 1½ cm. from the anterior border of the process, and when located the nerve should be gently drawn forward, as the jugular vein will be found ½ cm. to its inner side. The nerves accompanying the sinus through the posterior lacerated foramen are covered by it so that they need not be considered. The foramen magnum lies 1½ cm. to its inner side and posteriorly. When the sinus is opened, slits of the inferior petrosal and occipital sinuses and the condyloid vein can be seen where these vessels enter the jugular vein. The jugular fossa, which contains the bulb of the vein, varies in shape in different skulls and on both sides of the same skull. At times it is vaulted and smooth and approximates the floor of the middle meatus, but it may be low, contracted, and traversed with irregular ridges. The former condition is considered a predisposing cause in thrombosis of the bulb of the jugular vein on account of the more intimate relation of this part with the

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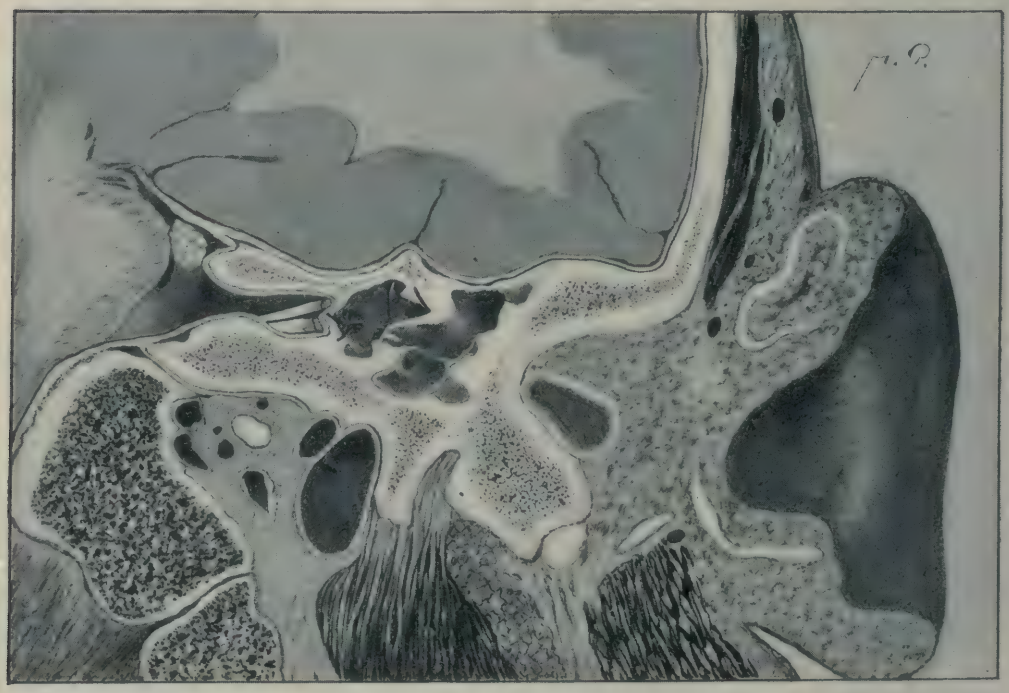
EXPLANATION OF FIG. 8.

Deep dissection of temporal bone, with osteoplastic flap of squamous plate, exposing dura mater, carotid artery, entire course of facial nerve in temporal bone, giving off the superior petrosal nerve at its bend above the middle meatus; turns of the cochlea between the facial nerve and carotid artery above, and the vestibule with superior and exterior semicircular canals, and antrum, posteriorly. The remaining portion of inner wall of middle meatus shows opening of Eustachian tube in front and fenestra ovale and rotundum behind. Below these the sigmoid flexure of the lateral sinus is seen in the openings of the posterior condyloid vein and inferior petrosal sinus.



EXPLANATION OF FIG. 9.

Cross-section of right side of head, showing external meatus, separated from middle meatus by outer wall of atticus above and tympani muscle below. On the middle meatus are seen the tegmen tympani, the ossicles, the tensor tympani muscle, and projections of the aqueductus Fallopii, with facial nerve above and first turn of cochlea below. Deep in the bone the cochlea. Below, the bulb of the jugular vein.



EXPLANATION OF FIG. 10.

Cross-section of left side of head, 1 cm. behind previous section. A small portion of the posterior wall of external meatus is seen. Internal to this, the tegmen, aditus ad antrum, projections of external semicircular canal and posterior wall of middle meatus. The vestibule shows bristles coming from the superior and external semicircular canal. The internal meatus contains the facial and auditory nerves. Below is seen the jugular vein with openings of the posterior condyloid vein and inferior petrosal sinus.

middle meatus; and the same is also claimed, on account of the more tortuous course the blood stream is subjected to. Infectious material might pass along the entire route of the sinus without producing any harm, but at the jugular fossa the flow of venous blood is checked, producing currents (whirlpool) which favor the formation of a thrombus, on account of the greater liability to injury and infection which the wall of the vein is subjected to.

If the bulb of the vein alone is involved, the jugular should be ligated before the sinus and bulb are incised; but if the infection has gone farther, and a cord-like strand on the side of the neck indicates an extensive thrombus of the vein, ligation should not be performed.

To demonstrate the intimate relation between the ear and the cerebral cavity, a transverse section of the head through the centre of the middle meatus has been made (Fig. 9). The external auditory canal is seen slanting upward and inward, its outer half lined with short hairs directed outward. The external is separated from the middle meatus above by a plate of bone which forms the outer wall of the atticus, while below is the tympanic membrane, with the manubrium and processus brevis of the malleus attached to it. The roof of the middle meatus has a thin plate of bone, the tegmen tympani, separating it from the cerebral cavity.

A section of this kind demonstrates the intimate relation between the two parts and shows how readily an erosion or a fissure in the division line may lead to serious involvement of the brain and its covering when the middle ear is inflamed.

On the inner wall of the meatus can be seen, from above downward, first, the projection made by the aqueductus Fallopii with its facial nerve; underneath this the tendon of the tensor tympani muscle emerging from the upper part of the Eustachian tube. Directly behind it and on the same level is the fenestrum ovale, containing the stapes. From here on downward the promontorium, representing the beginning of the cochlea, bulges outward, forming a recess with the floor of the meatus. The floor consists of a varied thickness of bone and occasionally communicates with the jugular fossa through fissures or small lymph channels.

The cavity of the meatus contains the ossicles. Of these the malleus is anterior, with its head in the atticus, the tendon of the tensor tympani muscle attached to its neck, and the suspensory ligament extending from the tegmen to its head. Its short process projects outward, throwing the upper part of the membrane into folds, and the manubrium extends downward, with its tip turned outward, attached to the mid-point of the tympanic membrane. The incus is located posterior to the malleus, with its body in the atticus, its short process in the aditus, and its long process projecting downward and articulating



with the head of the stapes. The stapes is lodged in the fenestrum ovale, with the stapedius muscle attached to its neck posteriorly, and lies horizontally and at right angles both to the malleus and incus.

Internal to the middle ear and set in the most compact part of the petrous bone are the spiral turns of the cochlea, with the apex pointing out and forward and the base butting against the wall of the internal auditory meatus.

Below the bony framework surrounding the ear and lying somewhat to the inner side of the middle meatus is the bulb of the jugular vein, in the jugular fossa.

A transverse section of the head, about 1 cm. behind the one just described (Fig. 10), shows only a small portion of the posterior wall of the external meatus, and parts of the middle and inner meatus corresponding to that level. Above, a thin plate of bone is seen separating the cerebral cavity from the aditus ad antrum. The aditus, shaped like an inverted pyramid, has the protrusion of the horizontal semicircular canal forming a part of its floor and inner wall. Below this is seen the posterior wall of the middle meatus proper, made up of irregular, open bony cells covered with a delicate mucous membrane, which lines the meatus and communicating cavities. Internal to these parts can be seen the interior of the vestibule, with the openings of the semicircular canals on its outer side. Anteriorly, the anterior ends of the superior or vertical and the external or horizontal canals have a common opening, while posteriorly the posterior end of the superior and the upper end of the posterior canals have a common opening. The openings of a horizontal canal lie on the same plane, while those of the posterior canal lie one above and the other below the posterior opening of the horizontal canal (Fig. 12).

The exterior of the superior or vertical semicircular canal forms a slight protuberance on the upper surface of the petrous bone corresponding to its course, from in front and externally, back and internally.

Internal to the vestibule is the internal auditory meatus containing the facial and auditory nerves; the facial above, directed toward the aqueductus Fallopii, and the auditory below, about to enter the vestibule and cochlea.

EXPLANATION OF FIG. 11.

The dura mater of the middle fossa of skull is cut away, showing a dissection of the temporal bone. From without inward are seen the mastoid antrum behind, the middle meatus with ossicles in front, and the aditus ad antrum between. The vestibule shows the openings of the semicircular canals. The facial nerve has the superior petrosal nerve coming from its bend and passing inward. In front of the nerve the tensor tympani muscle is seen in the Eustachian tube; behind it, the cochlea and internal auditory meatus. Internal to these the carotid canal, the carotid artery, and the Gasserian ganglion. Posteriorly the lateral and superior petrosal sinus have been slit open. The seventh and eighth nerves are seen entering the internal auditory meatus; the ninth, tenth, and eleventh the jugular fossa.



The bulb of the jugular vein is seen in the fossa, and several slits indicate the entrance of emissary veins.

On inspecting the middle and posterior fossa of the skull, when the brain has been raised from its bed, and removing the dura mater over the petrous bone in the middle fossa, the following structures can be exposed by chiselling the bone (Fig. 11): Externally, the mastoid antrum; in front of it, and coming from the middle meatus, the aditus ad antrum. The horizontal semicircular canal is seen helping to form the inner wall and floor of this passage. The middle meatus is anterior and internal to the antrum, and presents the malleus and incus in the atticus, and the tympanic membrane deep down, forming its outer wall. The tensor tympani muscle is seen in its groove in the upper part of the Eustachian tube, passing outward and backward, and becoming inserted into the neck of the malleus. The facial nerve is seen as it disappears at the upper anterior angle of the middle meatus, forming an elbow from the angle of which the superior petrosal nerve is given off. Posterior to this point it lies between the cochlea, which is on its inner and the vestibule, which is on its outer side. In the internal auditory meatus it lies above the auditory nerve, and in the posterior fossa to its outer side.

The vestibule shows the groove of the superior semicircular canal and the openings of the other two canals. The cochlea lies in the back part of an angular recess formed by the bend in the carotid canal as it ascends from the base of the skull, and has the tympanic cavity and aqueductus Fallopii, with the facial nerve to its outer side. The Eustachian tube is in front, the internal auditory meatus behind, and the compact bone over the carotid canal to its inner side.

The carotid canal has the general direction of the petrous bone inward and forward, with the Eustachian tube immediately in front of it, the superficial petrosal nerve coursing over it as it passes from the hiatus Fallopii to the middle lacerated foramen and compact bone behind it. As it ascends from the base of the skull it is directly internal to the inner wall of the middle meatus. As the canal passes inward toward the middle lacerated foramen, the Gasserian ganglion lies over it, in a depression at the inner end of the superior surface of the petrous bone.

The middle meningeal artery can be seen through the dura mater as it emerges from the foramen spinosum, and sends its anterior and

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EXPLANATION OF FIG. 12.

Anterior-posterior section through middle meatus. On inner wall of middle meatus are seen the opening in processus cochleariformis and Eustachian tube in front; facial nerve behind, and fenestrum ovale and rotundum, with promontorium below. Above the middle meatus are seen the superior, external, and posterior semicircular canal and superior petrosal sinus. Below are the styloid process, stylomastoid foramen, and jugular vein. Also cerebrum, tentorium cerebelli, cerebellum, and lateral sinus.

posterior branches outward and upward, grooving the skull in its course. The superior petrosal sinus is seen running along the superior posterior border of the petrous bone, joining the lateral with the cavernous sinus.

The lateral sinus extends from the torcular Herophili behind to the jugular foramen in front. At the torcular it communicates with the lateral sinus of the other side, the longitudinal sinus above, and the occipital below. The part which descends from the horizontal limb to the jugular foramen is known as the sigmoid flexure of the lateral sinus. It forms an elbow with the horizontal limb, and passes downward and inward in the deeply grooved bone until it reaches the posterior lacerated foramen, where it is joined by the inferior petrosal sinus and the posterior condyloid vein to form the internal jugular vein. It is accompanied by the ninth, tenth, and eleventh nerves.

If a vertical antero-posterior section of the head is made to pass directly through the tympanic cavity (as seen in Fig. 12) the following points of interest can be shown: Between the tympanic and cerebral cavities the tegmen tympani, on the inner wall of the middle meatus, which is covered by delicate mucous membrane, the orifice of the Eustachian tube and the canal for the tensor tympani muscle (processus cochleari formis); the latter has an orifice at its posterior end, and transmits the tendon of the tensor tympani muscle; behind this the aqueductus Fallopii, with the facial nerve passing back and down, around the fenestrum ovale; underneath this the promontorium, with the fenestrum rotundum. Projecting from the floor downward is the styloid process. Below this is a section of the jugular vein.

Above and posterior to the middle meatus is the body of the petrous bone traversed by the semicircular canals. The openings of the horizontal or external one are above and parallel to the facial nerve; the vertical or superior passes from in front upward and posteriorly; the posterior canal is situated behind, with one opening above and the other below the posterior opening of the horizontal, as mentioned previously.

At the upper posterior border of the petrous bone is the superior petrosal sinus. A part of the sigmoid flexure of the lateral sinus is seen at a point where the occipital meets the petrous bone. The opening of the lateral sinus is seen behind at a point where the tentorium cerebelli meets the dural lining of the occipital bone. The tentorium is seen separating cerebral from cerebellar convolutions.

In recapitulating the operative technique mentioned in the foregoing pages five separate procedures may be described:

First, "radical" exposure of the middle ear; second, exposure of the mastoid antrum; third, exposure of the mastoid antrum and cells and lateral sinus ("mastoid quadrants"); fourth, exposure of the

temporal lobe of the brain and middle fossa of the skull; fifth, exposure of the occipital lobe of the brain, tentorium cerebelli, cerebellum, and posterior fossa of the skull.

For the "radical" exposure of the middle ear an incision is made ½ to 1 cm. behind the attachment of the auricle extending from above the ear downward to the tip of the mastoid process (Fig. 1). Above the temporal ridge, which corresponds in height to the upper wall of the outer meatus (Fig. 2), the incision should be through skin and superficial fascia alone, leaving the temporal muscle intact. Below the ridge it should pass directly to the bone. The tissues are dissected forward and the periosteum elevated until the bony meatus is reached. To avoid possible necrosis of the tympanic plate the soft parts of the posterior and upper wall of the soft meatus alone should first be detached with an elevator and then incised by means of a thin-bladed knife near the tympanic membrane and held against the anterior wall with a long, narrow retractor; or, if the tympanic plate is to be chiselled away, the anterior and lower walls can be cut also and the entire funnel of soft tissues drawn out of the bony canal and retracted with the auricle. The tympanic membrane is now cut from its ring of bone and removed with the malleus after the attachment of the tensor tympani muscle has been severed. With a chisel, or preferably a burr drill, the outer wall of the attic, which corresponds to the inner part of the upper wall of the external meatus, is then removed until the roof of the attic is continuous with the upper wall of the external meatus (Figs. 4 and 5). If this does not give a sufficient exposure the tympanic plate can be chiselled away as far as the styloid process (Fig. 6). After removal of the incus (Fig. 5), which should be cautiously done, so as not to dislodge the stapes from the fenestrum ovale, a probe should be passed through the aditus into the antrum, and the bone chiselled or drilled away external to it (Figs. 6 and 7). The interior of the cavities are now curetted and smoothed, care being taken not to open the aqueductus Fallopii and horizontal semicircular canal, nor to dislodge the stapes. If the tegmen is necrosed, this should be removed, but puncture of the dura mater should be avoided. An extradural, intradural, or cerebral abscess can be located or drained through this aperture, but a trephine opening through the squamous plate of the temporal bone, after the temporal muscle has been detached and drawn upward, is better for this purpose (Fig. 6). The latter will also suffice for aspirating the lateral ventricles for excessive accumulation of cerebro-spinal fluid. If a deep dissection of the temporal bone is necessary, especially if the upper surface of the petrous bone is to be exposed, or if an abscess is not drained sufficiently through the trephine opening just mentioned, a quadrilateral osteoplastic flap, 3 cm. wide and 4 cm. long, with its base anteriorly, should

be made to include the portion of squamous bone lying over the posterior half of the zygomatic arch, and reaching back as far as the middle of the mastoid process (Fig. 8). If the upper portion of the petrous bone is to be chiselled, the dura mater should be elevated gently and the brain retracted with a broad, blunt retractor. More room can be obtained by incising the dura and permitting some cerebro-spinal fluid to escape. This should not be done if pus is present or if the brain or its coverings have not already been attacked. After the tissues have been replaced to their original position and sutured, an opening is left sufficiently large for drainage, and the wound packed with gauze until epidermization of the exposed parts is complete.

To expose the mastoid antrum an incision is made ½ to 1 cm. behind the auricle, extending from a point corresponding in height to the upper wall of the external meatus downward to the tip of the mastoid process (see cross on Fig. 1). The tissues are dissected forward and the periosteum elevated until the suprameatic spine can be felt with the finger or an instrument. Keeping below the temporal crest, an opening is made with a chisel or burr drill 1 cm. behind the suprameatic spine. The instrument should be directed forward, inward, and slightly upward, corresponding to the direction of the external meatus to a depth of 1 to 2 cm. When the instrument has penetrated deeper than 1½ cm., care must be taken not to open the horizontal semicircular canal or aqueductus Fallopii. When the antrum has been reached, granulations or irregular bony ridges should be removed by means of a curette, care being taken to avoid piercing the tegmen antri above or the bone behind which separates the antrum from the lateral sinus. If the latter be exposed no harm need necessarily result, but if punctured, the hemorrhage must be controlled by packing the bony wound with a graduated gauze tampon. When the antrum is clean and smooth the parts are replaced and sutured, leaving an opening for drainage. When the cavity is again in a healthy condition the opening will close by granulation, or a small plastic operation will be required to effect this.

If the lateral sinus is to be exposed with the antrum and mastoid cells, the mastoid process should be divided into four quadrants, as described previously (Figs. 3 and 4). The anterior superior quadrant is opened first with the instrument directed as mentioned in the previous operation, and the antrum cleaned and packed. Next, the two lower quadrants should be opened and evacuated. After packing these to prevent inflammatory discharges from spreading, the upper posterior quadrant should be entered and the lateral sinus exposed. Here the instrument, preferably a burr drill, should be directed straight in. Palpation of the sinus must be performed very carefully, in order not to dislodge adherent or incomplete thrombi. In such a case, aspira-

tion with a hypodermic syringe might show blood and lead to an erroneous diagnosis, so that an exploratory incision is safer. For this purpose the lower posterior quadrant should be drilled sufficiently deep to expose the sinus below, and the ledge between the upper and lower quadrants should be removed in order to make them continuous.

To expose the entire sigmoid flexure of the lateral sinus and the bulb of the jugular vein, the lower portion of the mastoid process must be removed (Fig. 8). The facial nerve should be located and exposed to its exit at the stylomastoid foramen, and the spongy bone between it and the sinus chiselled away. Posteriorly the foramen magnum must be avoided. If the thrombus is still confined to the upper portion of the jugular vein, ligation should be performed below this point before the sinus is incised.

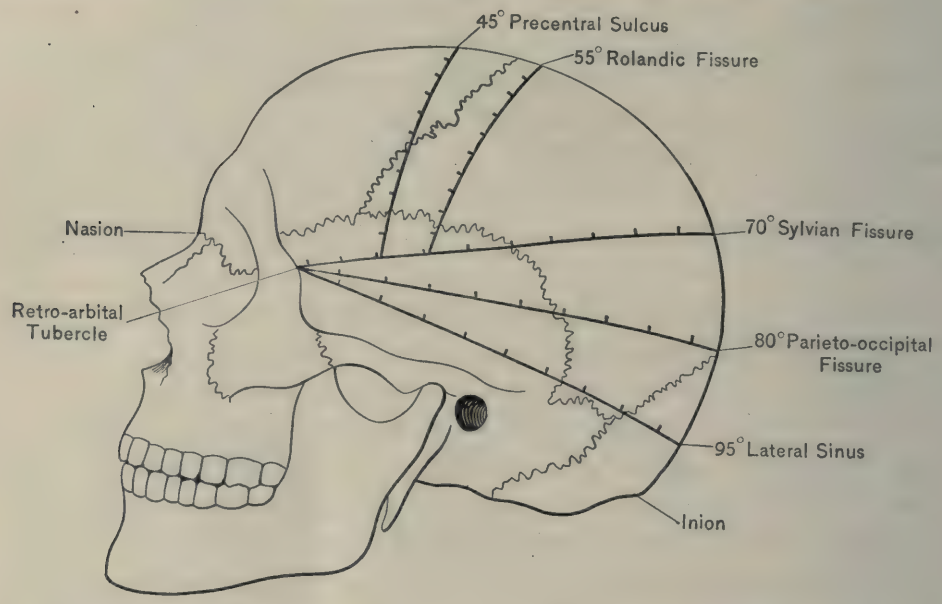
If the horizontal limb of the sinus is to be exposed, an incision from the upper posterior quadrant, first upward and backward, and then downward and backward toward the external occipital protuberance, is to be made (Figs. 5 and 6). A strip of bone is then removed by means of a chisel, circular saw, or drill, and the sinus incised to the extent of the clot. Hemorrhage is to be controlled with gauze strips or compresses, the former to be introduced directly into the lumen; or, if this is insufficient, compression should be applied to the external surface of the sinus after detaching it from its bony casing. The parts are subsequently replaced and sutured, a sufficient opening being left for drainage.

To expose the occipital lobe of the brain, the cerebellum, or posterior fossa of the skull, a single or double "trap-door" incision is made above and below the lateral sinus (Fig. 7). To locate the latter, Chipault's method can be applied. It consists in taking 95 per cent. of the distance between the nasion and inion, and joining this point with the retro-orbital tubercle. The posterior half of the line represents the horizontal limb of the lateral sinus.

The incision through the bone is made by means of a circular saw, a drill, or Gigli's wire saw, and trephined. The base of the bony flap is to be nicked on either side with the chisel, so that the bone will break off in a straight line when pried open with the elevator. The dura is to be incised in the same direction as the outer flap, a sufficient margin being left if the condition found permits subsequent suturing.

Other points of interest in cranial topography are located by the same method just mentioned (Chipault's), to wit: A point 80 per cent. of the distance between the nasion and inion joined with the retro-orbital tubercle represents the course of the parieto-occipital fissure. A point 70 per cent. the distance of the same sagittal line joined with the tubercle represents the course of the fissure of Sylvius. If the latter be divided into tenths, and the junction of the third and fourth tenth be

joined with the 55 per cent. point on the longitudinal line, the course of the Rolandic fissure is shown; and if the junction of the second and third tenth on the Sylvian line be joined with the 45 per cent., the precentral fissure is indicated. The middle meningeal artery crosses between the second and third tenths of the three primary lines.



In conclusion, I wish to express my indebtedness to Professor Frank Hartley for the many valuable suggestions offered during the progress of this work. I also wish to acknowledge the painstaking efforts of Mr. M. Peterson, draughtsman for the anatomical department, in producing anatomical accuracy in the accompanying drawings.

GANGRENOUS CHOLECYSTITIS, WITH A REPORT OF A CASE IN WHICH A SUCCESSFUL CHOLECYSTECTOMY WAS DONE.

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Gangrenous cholecystitis is a pathological condition sufficiently rare to warrant the report of every case. It may be looked upon as an extreme degree of phlegmonous cholecystitis, which is more frequently met with, but this condition usually results in death before a true gangrene of the gall-bladder is established. Robson, in the second edition of his book on *Diseases of the Gall-bladder and Bile Ducts*, speaks of gangrenous cholecystitis as "extremely rare," and says that he has been able to find but one case reported, that of Hotchkiss

(*Annals of Surgery*, February, 1894). Robson, however, reports a case of his own which might be classed under this head. In the second edition of Kehr's book can be found no mention of a case of gangrenous cholecystitis. Mayo, however, has reported one case in which the gall-bladder was successfully removed. Including Mayo's second series (*Annals of Surgery*, June, 1902), in which no such case is reported, it may be stated that there was only one case in 433 operations upon the gall-bladder and ducts, performed by W. J. and C. H. Mayo. These statements show the great rarity of a true gangrenous cholecystitis. Before discussing the condition I will briefly report a case in which the gall-bladder was successfully removed.

The patient, a woman, aged fifty-two years, was admitted to the Polyclinic Hospital on October 3, 1902. There was nothing in her previous history worthy of note excepting that she had suffered from frequent attacks of indigestion accompanied by nausea and vomiting. During these attacks she had been able to retain practically no food. The pain had never radiated to the shoulders, nor had the patient ever been jaundiced.

Her present illness began three days before admission, with pain in the left hypochondriac region and vomiting. These symptoms kept up intermittently. I saw the patient on the evening of October 3d. At this time she had a temperature of 102° F., pulse of 112, and respiration of 32. She complained of pain and tenderness on the right side of the abdomen, but these were less severe than they had been; the bowels were constipated. There was considerable rigidity of the abdominal muscles on the right side, and a tumor was palpable, which was smooth and which seemed to move away from the examining hand. I was asked to see the case as probably one of appendicitis, but the position and condition of the tumor convinced me that the case was not one of appendicitis. The next morning the leucocyte count was 37,600. At this time there was more tenderness and more rigidity; so much more in fact that the tumor could not be palpated. Immediate operation was determined upon.

When the patient was anæsthetized and the abdominal muscles relaxed it was easy to diagnose a distended gall-bladder. An incision was made over the tumor, and when the abdominal cavity was opened some free fluid was found. The gall-bladder was covered by an adherent omentum, which, when removed, showed the organ to be distended and its entire fundus of a dark purple color. A number of large abdominal pads were inserted, the gall-bladder incised, and a quantity of very foul pus evacuated. The mucous membrane was green and gangrenous throughout. A large stone was found fixed at the mouth of the cystic duct. The whole fundus of the gall-bladder was gangrenous through all its coats. The line of demarcation between this and the remaining portion of the gall-bladder was very clear. This portion was quite thin, but the rest of the organ was very much thickened, measuring from one-half to one inch, as is shown in the accompanying photograph. It was decided to remove the gall-bladder, and its separation from the liver was easily accomplished by means of the finger, the tissues being soft from infil-

tration; no bleeding resulted from this separation. When an attempt was made to pass a ligature about the cystic duct the gall-bladder separated and came away. This took place when very little traction was being made upon it before the first knot in the ligature was tied, which well illustrates the condition of the organ even as low down as the cystic duct. The cystic artery bled freely and could not be controlled by a hæmostat, as the instrument cut through the inflamed tissues. Gauze packing was then introduced and controlled the hemorrhage absolutely. A number of large gauze drains were inserted and the wound partially closed. The patient was very ill soon after the operation, requiring hypodermoclysis, but her condition quickly improved, and the next day she was in fairly good condition. Convalescence was uninterrupted, the wound healing rapidly. An



Due to the contraction of the gall-bladder, it was impossible to replace the stone in its original position at the mouth of the cystic duct.

interesting feature in the convalescence, however, was the leucocyte count. This stood at 37,600 on the morning of the operation; the next day it had dropped to 12,600; the count then rose again to about 15,000 to 18,000, and finally gradually subsided. The patient was discharged from the hospital on November 14th, with only a small superficial granulating surface remaining. This subsequently entirely healed.

The etiology of gangrenous cholecystitis rests probably on two factors, obstruction of the cystic duct and infection by virulent micro-organisms. Whether either of these alone would produce it could hardly be proved, since in all cases micro-organisms are present and

some form of obstruction, though it may result only from a swollen mucous membrane. It is hard to believe that gangrene of the organ could develop with a patulous cystic duct. Of course, gangrene of the gall-bladder does not occur until the inflammation has obstructed the circulation, and the fact that the gall-bladder is so well supplied with bloodvessels saves it from gangrene, no doubt, in many instances. The pathological lesions of the gall-bladder closely resemble those of the appendix, but gangrene of the one organ is rare and of the other common, and in all likelihood this is to be attributed to the poor blood supply of the one and the free blood supply of the other. In the case reported the cystic artery bled freely when the gall-bladder was removed, and yet the entire mucous membrane and all the coats of the fundus were gangrenous. In this case I believe gangrene resulted from the firm impaction of the large stone at the mouth of the cystic duct, cutting off, when inflammation became well established, the circulation in much the same manner as an appendolith does in the appendix. The way in which the omentum was found spread over and adherent to the fundus of the gall-bladder reminded one of the way in which it so frequently surrounds a gangrenous appendix.

Of the symptoms it will suffice to refer to those presented in the above case. In brief, they are those of a violent, localized peritonitis, with usually some temperature, persistent vomiting, obstruction of the bowels, and a high leucocyte count. Jaundice is not generally present unless there exists a marked cholangitis, or unless the inflammation has extended by contiguity into the liver structure.

The diagnosis of this condition may be confused with that of appendicitis. When an anæsthetic is administered, however, I believe that the two conditions can be differentiated and certainly immediate operation is equally called for in both. It would be a serious error to delay the opening of the abdomen in order to make a differential diagnosis between these two conditions.

The question of treatment probably ranks in interest next to the pathology. With the symptoms referred to no surgeon would hesitate to urge immediate operation, exactly as he would in the presence of similar symptoms referable to the right iliac region, and I believe that precisely the same treatment should apply to a gangrenous gall-bladder as applies to a gangrenous appendix. Some authorities have in phlegmonous inflammation of the gall-bladder recommended and practised simple drainage. This may be good surgery when the stage of gangrene has not been reached, or when the organ is small and contracted and its removal might result in death from shock, the result of a prolonged operation; but when the entire mucous membrane is gangrenous, and particularly when a portion of the whole thickness of the wall of the gall-bladder is gangrenous, total removal of the organ

is called for, and to leave it would be comparable to leaving a gangrenous appendix which had been freed from all its adhesions and lay well separated from the abdominal cavity by gauze pads. To drain and leave such a gall-bladder means continued absorption and probably an early death from sepsis. The relief following the removal of an organ in such a condition is well illustrated in my own case by the immediate cessation of symptoms and a fall in the leucocyte count from 37,600 to 12,600 in twenty-four hours. Regarding the technique of the procedure of cholecystectomy in the presence of inflammation of even a milder type than was here present, I am convinced that the advice of Mayo, who states that the cystic duct should not be ligated, is sound, and I am exceedingly glad that in my case the gall-bladder separated and came away before I committed what I now believe would have been an error. There must, in all such cases, be considerable cholangitis present, and nothing gives such relief in this condition, or so quickly arrests it as external drainage.

JAUNDICE, WITH REPORTS OF INTERESTING ILLUSTRATIVE CASES—A CONTRIBUTION TO THE TOXIC FORMS OF THIS CONDITION.*

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Most writers upon the subject of jaundice arrange all cases under two heads—obstructive and non-obstructive, or extrahepatic and intrahepatic jaundice. The data at hand, however, are insufficient to permit of a clear discrimination and an accurate classification in this manner. Furthermore, several possible causes may exist in a given case of jaundice, and it is often difficult to discover which of these is the preponderating or active factor in the condition. In certain cases of obstructive jaundice there is associated a pathological condition of the blood, or of the hepatic cells, one or both. Hence, the great variety and uncertainty of the causes prevent a satisfactory classification at present writing.

There are few diseases of the liver and of the bile passages that are invariably unattended by jaundice. In this group, however, may be placed amyloid liver and fatty liver. On the other hand, there are many hepatic diseases and conditions in the course of which jaundice may rarely occur. Among rare instances may be mentioned chole-

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cystitis, needles, fruit-kernels, distomata, and round worms in the choledoch duct; echinococci, stagnation of bile in the intrahepatic biliary passages, in consequence of interference with the descent of the diaphragm (as in diaphragmatic pleurisy on the right side), so that the propulsion of the bile from the liver to the intestine does not occur (Schuppell); inspissated bile, lipoma, and polypus growing from the wall of the biliary canal, secondary syphilis, and, finally, kinks in the common duct in consequence of displacement of the liver. Frerichs[1] speaks of jaundice caused by an accumulation of pigment in the canaliculi lying between the hepatic cells, as, for example, in malignant malarial fevers; also of an etiological variety occasioned by hemorrhage that drains the vena porta, as in yellow fever. In the latter event there occurs disturbance in the hepatic circulation, with abnormal diffusion of bile and, at times, jaundice. That a paralytic and spastic jaundice occurs, as the older writers contend, is more than doubtful. The commoner causes for both intrahepatic and extrahepatic jaundice are too well known to require enumeration here. Besides, I purpose to consider principally so-called toxic jaundice, giving brief notes of a few illustrative cases. It is sometimes impracticable to distinguish clinically between instances of toxæmic origin and those due to obvious obstruction. Moreover, the fact that, as previously stated, the different forms, etiologically considered, may co-exist is to be recollected.

In the course of numerous affections that are accompanied by profound toxæmia jaundice may be observed. The toxic form also arises from the action of certain poisons, as ether, chloroform, and the like. The question, Is there a true toxæmic or diffusion icterus? is no longer, as formerly, a vexed one. A number of hypotheses, however, have been advanced to explain its occurrence, with doubtful justifications in most instances. Liebermeister contends that under conditions of pathological change the liver cells cannot retain their secretions.

The theory of Cornil[2] probably explains the mode of origin of many cases at least; it is that the epithelial lining of the smaller bile ducts becomes swollen, and an obstruction is thus produced.

Within the past few years I have met with cases, some of which are reported below, that apparently tend to support in the main the view advanced by Frerichs, and upheld by Murchison,[3] that in many instances of toxic jaundice an excessive amount of bile pigment is secreted, with subsequent reabsorption of the redundant quantity from the intestines. It will be seen later that while the primary and striking pathological feature may be found in the blood, and the amount of bile secreted may be in excess, there is probably in all such cases of jaundice temporary obstruction in the fine biliary canals as the result of increased viscosity of the bile or an intrahepatic cholangitis; hence, reabsorption, not from the intestines, but from the liver, occurs. That

we have no means of determining with accuracy the quantity of bile generated per diem, however, is generally conceded, so that this theory lacks demonstrative proof; it rests solely upon clinical testimony. On the subject of polycholia due to ether narcosis, which falls under this head, the literature is peculiarly silent; this is even more true as regards the report of any undoubted cases. In this connection the case of jaundice reported below, following the anæsthetic state, seems worthy of being recorded:

CASE I.—Mrs. A. M. S., aged twenty-six years, childless, an actress, was admitted to the gynecological wards of the Medico-Chirurgical Hospital February 27, 1902, under the care of Dr. W. Easterly Ashton.

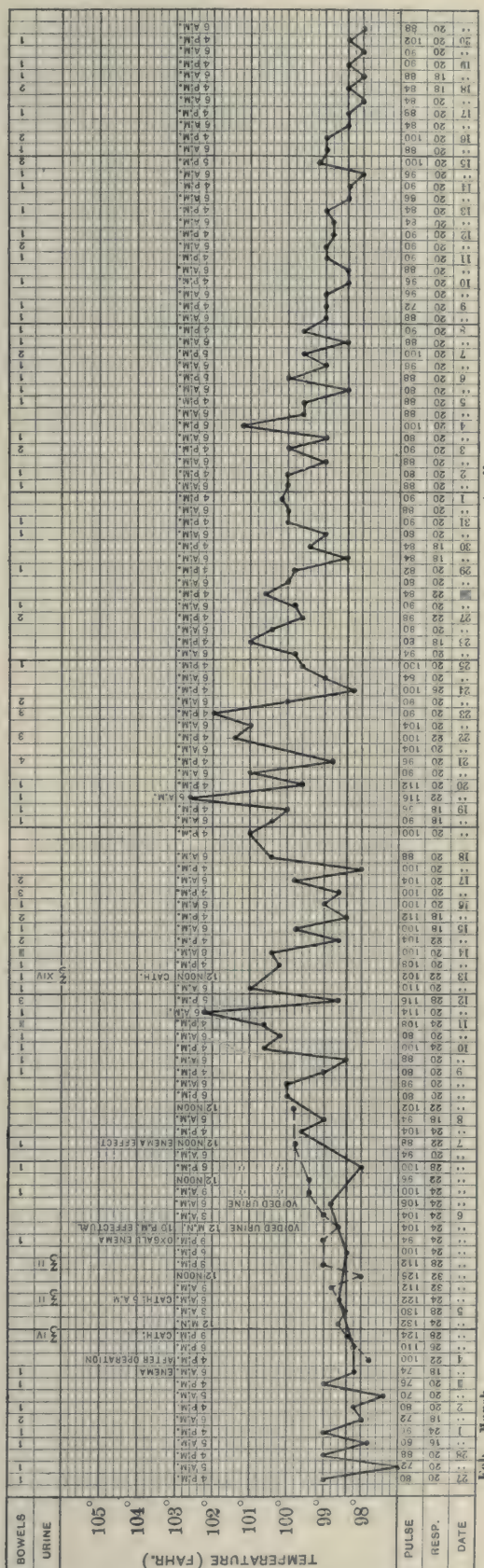
The family history revealed the death of the father from smallpox; also that of the mother from some unknown cause, and of one aunt who died of chronic Bright's disease. The patient had had some of the diseases of childhood; malaria at fourteen, with occasional recurrences since then; peritonitis when sixteen years old, lasting four months; from the age of thirteen until the present she has had tonsillitis at intervals. Since the attack of peritonitis the menstruation has been both profuse and painful. In September, 1901, she suddenly developed acute gastric symptoms, as eructations, with severe pain in the epigastric and the right hypochondriac regions. No history of jaundice appeared that could be elicited now, and the duration of the illness was about one week.

On admission (February 27th) the patient presented the symptoms of bilateral ovarian disease, and on March 4th was operated upon by Dr. Ashton. Cœliotomy revealed a pyosalpinx on one side and a hydropyosalpinx on the other. The case progressed favorably until March 7th (except for persistent vomiting, with retching, in consequence of the etherization), when there appeared slight fever and distress after the feedings; slight pains referred to the epigastrium, right hypochondrium, and the region of the small intestines. Up to this time the bowels had been confined, but now, as the result of a mild saline laxative, diarrhœa set in and soon became a troublesome symptom, there being six to eight movements in the twenty-four hours. The dejecta were of a dark greenish-yellow color in appearance, not offensive, and apparently contained much bile.

On March 12th jaundice appeared, but was slight; the next day the skin and scleræ showed a distinct, moderately deep, saffron hue, not much gastric but more intestinal disturbance, and low irregular fever. (See temperature Chart 1.) The physical signs indicated slight enlargement of the liver; moderate tenderness to palpation over the liver, more marked over the gall-bladder area and intestines. The abdominal wound was reported to be in good condition. Bradycardia absent. The urine analysis showed the presence of bile-pigment, traces of albumin, and a few narrow granular casts. In color it was a dark greenish-yellow, and when shaken displayed a yellow froth.

March 14th. Some pain, which at times radiates to the right shoulder and down the right flank, and tenderness over the region of the gall-bladder, but this organ could not be felt. The jaundice continued, and the urinary examination gave the same result as noted above. The stools still numbered six to eight daily, and were deeply bile-

CHART 1.


BOWELS
URINE
TEMPERATURE (FAHR.)
105°
104°
103°
102°
101°
100°
99°
98°
PULSE
RESP.
DATE
Feb. March
April
VOIDED URINE
ENEMA EFFECT
CATH.
ENEMA
AFTER OPERATION
OXSALIC ENEMA
CATH. 5 A.M.
VOIDED URINE 12 M.N.] 10 P.M. EFFECTUAL

stained. The blood examination gave the following result: Red corpuscles, 3,090,000; hæmoglobin, 60 per cent.; white corpuscles, 27,000. The increase in leucocytes affected principally the polymorphonuclear elements—a simple leucocytosis. A few poikilocytes and nucleated red cells were noted. March 17th, the jaundice and the local symptoms began to disappear.

19*th.* The skin and conjunctivæ are almost free from discoloration; neither bile, albumin, nor casts were present in the urine, but the bowel movements are still frequent, seven to eight per day; dark greenish-brown in color and, on testing, contained bile pigment.

20*th.* Jaundice practically absent, patient comfortable except from pain in lower abdominal region. The stools were less frequent—three to four daily, and they contained less bile. About this time, or possibly a couple of days earlier, an abscess in the wound was discovered and properly treated.

April 4*th.* The patient's general condition greatly improved, the bowels were moving once or twice daily, and the stools presented a normal appearance. An examination of the blood resulted as follows: Red cells, 3,730,000; whites, 20,000; hæmoglobin, 69 per cent. The case is well advanced in convalescence, as the temperature chart also corroborates. At no time during the course of the jaundice was bradycardia present.

The nature of the jaundice in this case is difficult to determine. Was it a case of polychromia or polycholia? In this condition the jaundice results from the dissolution of red blood corpuscles, whereby a large amount of hæmoglobin is set free in the blood current and is converted by the liver cells into bile pigment. The increased formation of bile pigment is invariably attended with increased viscosity of the bile, and the altered, inspissated, hepatic secretion opposes a temporary obstruction to the onward movement of the bile, followed by its absorption. This position is pretty firmly established from the experimental side by the labors of Stadelmann,[4] W. Hunter, Minkowsky and Naunyn.[5] Minkowsky and Naunyn submitted geese and ducks to the action of arseniuretted hydrogen, both before and after extirpation of the liver, and found that while hæmoglobin is present in the urine after removal of the liver, bilirubin is always absent.

Commenting upon the more recent experimental investigations into so-called "hematogenous" jaundice, Lazarus-Barlow[6] states: "It is now generally, though not universally, held (1) that a hematogenous jaundice does not exist; (2) that all varieties of jaundice are hepatogenous and due to reabsorption of bile formed in the liver; (3) the reabsorption is due to the presence of an obstruction in the bile ducts, whether this obstruction is obvious—*e. g.*, a gallstone—or not. Jaundice, therefore, only occurs as the result of blood destruction, when the liver seizes on the blood pigment, converts it into bile pigment, and returns it in bile to the blood." Since neither the polychromia nor the polycholia would occur without the primary blood destruction

in these cases, Murchison has suggested that the term "hematogenous" is appropriate in a certain sense, at least.

The evidence before adduced renders it certain that in all cases of jaundice an impediment to the onflow of the bile exists, or, in other words, that the liver is necessary to the production of jaundice. The term "hepatogenous" jaundice may be, therefore, appropriately applied to this symptom in every instance, but it seems to me that it would be advisable to regard as obsolete the term "hematogenous" and to retain that of "toxæmic jaundice" to designate such cases of hepatogenous form as that reported above, as well as all others in which blood destruction is a strong pathological feature. The increased hæmolysis in my case, if it actually existed, was most probably due in great part to the ether. The question, however, arises, Was not the jaundice dependent upon a cholecystitis associated with biliary obstruction? While some of the clinical symptoms and signs bore a close resemblance to cholecystitis, the nature of the dejecta and the brevity of the attack would tend to exclude the latter affection.

Moreover, the local phenomena were scarcely of sufficient intensity to warrant a diagnosis of suppurative cholecystitis; and the physical signs were too indefinite to be of diagnostic value. Again, owing to the slight suppuration in the wound, the presence of leucocytosis and irregular fever, the jaundice might be attributed to a septic process. It is to be recollected, however, that the slight septic symptoms persisted after the jaundice had disappeared. Moreover, in my experience, jaundice of the same degree of intensity has never occurred in so mild a grade of septicæmia. Was the patient affected with a duodenitis that acted as the causative factor? The usual section diet had been taken both prior and subsequent to the operation; it was not thought likely that this had produced duodenal catarrh. The presence of an apparently copious biliary secretion which was discharged per rectum also tends to exclude the possibility of the existence of obstruction in the common duct due to duodenitis. It was most probably true of my case that the abnormally large quantity of bile pigment suddenly generated occasioned an increased viscosity of the biliary secretion and consequent blocking of the hepatic canaliculi. This obstruction, however, was easily removed by a laxative, as compared with that due to catarrhal lesions, hence the comparatively short course of the jaundice. In my case bilious-looking stools promptly followed the administration of a saline laxative three days after operation.

As stated above, bradycardia was not present, while this symptom is the rule in instances of obstructive jaundice. The old view that bradycardia in pure hepatogenous jaundice is due to the action of the complete biliary secretion upon the heart, while in toxæmic jaundice the absence of the bile salts from the blood accounts for a normal

pulse rate in the latter variety, is no longer held. Strümpell contends that the infrequency of the pulse is due to the action upon the heart of the taurocholate of sodium. *Per contra,* as pointed out by Lazarus-Barlow, the assertion as to the absence of bile salts in toxic jaundice is not very reliable. Moreover, Stadelmann found them present in the non-obstructive jaundice caused by phosphorus, arseniuretted hydrogen, and other substances; and Naunyn found them in two cases of pyæmia in which the hepatic ducts were free. To account for the difference in respect to the pulse rate between toxic and hepatogenous jaundice is impossible at present writing. The extent of dissolution of the blood in the course of ether narcosis necessary to produce polycholia or polychromia is not known. The condition following the every-day run of operations is exceedingly rare, as shown by an examination of the literature. But that blood destruction occurs during the anæsthetic state has been absolutely proven. Da Costa and Kalteyer[7] have studied the blood in fifty cases, and have concluded that invariably etherization produces increased hæmolysis, following which the rapidly regenerated cells are imperfectly supplied with hæmoglobin. They believe that those who affirm the contrary are possibly misled by the blood concentration that results from the preliminary treatment which is often added to by the sweating during the anæsthetic state. These authors also maintain that the color index always falls and that the number of corpuscles always increases.

Through the kind aid of Dr. L. Napoleon Boston, I can give the results of a few experiments upon rabbits with ether administered by inhalation. The first series of experiments was upon two healthy female rabbits. The blood of each animal was examined directly before administering the ether, and again twenty minutes after the anæsthetic state was reached, at which time the ether was withdrawn. Forty minutes later (one hour after complete anæsthesia was reached) the blood was examined, and later daily until the animal's blood had returned to the normal.

Experiment I. Female rabbit, pregnant; weight 2 kilos, 130 grammes. Red cells, 4,462,500; white cells, 16,000; hæmoglobin, 60 per cent. Stained specimens presented nothing abnormal. Ether for twenty minutes (℥vj Squibb's). The red cells, 5,750,000; white cells, 24,000; hæmoglobin, 50 per cent. Red cells much distorted and presented decided variation in size, microcytes being numerous. A number of nucleated red cells (mostly normoblasts) were seen; many large polynuclear leucocytes showing irregular basophilic granules were observed.

One hour after ether: Weight 2 kilos, 110 grammes (lost 20 grammes). Red cells, 3,567,600; white cells, 24,000; hæmoglobin, 52 per cent. Poikilocytosis extreme. Microcytes and macrocytes numerous. Many crenated cells were seen in every field. White cells were at last noted.

Twenty-four hours after ether: Hæmoglobin, 30 per cent. Red cells are poor in staining properties, and often stain irregularly, some taking scarcely any of the eosin; poikilocytosis is marked. The polymorphonuclear leucocytes often contain large irregular granules, which are stained brownish by both the eosin and hæmotoxylin. Many cells resembling the "myelocyte" were also observed. Nucleated red cells (normoblasts) were not common.

Forty-eight hours after ether: Red cells, 4,500,000; white cells, 6000; hæmoglobin, 46 per cent. The red and white cells display but moderate variation from the normal. Seventy-two hours after ether, red cells, 4,980,000; white cells, 10,660; hæmoglobin, 47 per cent. One hundred and four hours after ether, hæmoglobin had reached 51 per cent., and on the following day 55 per cent. Otherwise normal.

Experiment II. Female rabbit, weight 3 pounds 3 ounces. Red cells, 3,960,700; white cells, 4200; hæmoglobin, 65 per cent. Twenty minutes after ether (℥iv Squibb's). Red cells, 4,375,000; white cells, 6500; hæmoglobin, 55 per cent. Poikilocytosis was marked, and crenated cells were not uncommon. Microcytes and macrocytes numerous. White cells appeared as normal.

One hour after ether: Weight 3 pounds. Red cells, 3,280,000; white cells, 8500; hæmoglobin, 58 per cent. Poikilocytosis extreme, and especially prominent is the variation in size of reds. Red cells do not stain equally. White cells, polynuclears, display many coarse, brownish granules. Nucleated red cells are not uncommon.

Twenty-four hours after ether: Red cells, 4,690,000; white cells, 6200; hæmoglobin, 43 per cent. Red cells stained irregularly, and many appeared as a mere shadow. Poikilocytosis was but moderate as compared to that observed in Rabbit No. 1. Crenated cells were common, as were also nucleated red cells. Forty-eight hours after ether: Hæmoglobin, 58 per cent. Otherwise as last noted. Sixty hours after ether: Red cells, 4,810,000; white cells 6800; hæmoglobin, 64 per cent. General appearance of stained specimens was as normal.

Experiment III. Female rabbit; weight, 1 kilo, 9845 grammes; was etherized for one hour, Squibb's ether (℥j) employed. Loss in weight 340 grammes. During the first twenty minutes hæmoglobin fell from 82 to 76 per cent., but at the end of an hour it had fallen to 72 per cent. During the following twenty-four hours the reduction in the hæmoglobin was very slight, and at the end of forty-eight hours it had returned to the normal. Leucocytes increased from 6200 to 13,000, while the red cells were, before ether, 6,230,000; twenty minutes after ether, 5,760,000; one hour after ether, 5,430,000; twenty-four hours after ether, 5,210,000; forty-eight hours after ether, 6,310,000; eight days after ether, 6,475,900. The changes in the stained specimens were practically those observed in connection with Experiment II., but were less pronounced.

With a view to determining as precisely as possible the effects of ether administered by inhalation upon the blood, a human subject was next selected, without any special preparation for an anæsthetic.

Experiment IV. J. H., male, aged thirty-three years. Irish extraction, who was apparently in perfect health, except for slight

ankylosis of the right knee, resulting from an injury, for which condition he was placed in my ward at the Medico-Chirurgical Hospital. His blood was examined May 1, 1902, which gave hæmoglobin, 86 per cent.; red cells, 4,280,000; white cells, 7600. Stained specimens were found to be normal in every respect. About five hours after a full meal (breakfast) he was given ether, Squibb's, for twenty minutes, at which time the ether was withdrawn and the blood examination repeated; hæmoglobin, 79 per cent.; red cells, 6,150,000; white cells, 16,000. There was no evidence of poikilocytosis; few microcytes were seen; all the erythrocytes stained normally. The increase in polymorphonuclear leucocytes was apparently well-marked. No myelocytes found.

An hour later, hæmoglobin, 74 per cent.; red cells, 4,170,000; white cells, 9800. Many of the red cells were seen to stain feebly with eosin, at times appearing as mere shadows, and there was decided variation in the size of the erythrocytes (microcytes). A differential count of the leucocytes gave polymorphonuclear, 81.91 per cent.; myelocytes, 4.94 per cent.; transitional, 10 per cent.; large mononuclears, 1.11 per cent.; small lymphocytes, 1 per cent.; eosinophiles, 1 per cent.

Twenty-four hours after ether it was reported that the patient had not vomited after the anæsthetic, and that he had taken food and drink twelve hours after the ether was withdrawn. His blood at this time gave hæmoglobin, 67 per cent.; red cells, 4,576,600; white cells, 13,600. Great variation in the size and staining properties of the erythrocytes was observed, and there was pronounced distortion of many of the larger cells. Certain cells stained unevenly, and the general appearance of these cells was not unlike those found in severe grades of anæmia. Leucocytes presented practically the same appearance noted at the previous examination.

Thirty hours after ether: Hæmoglobin, 78 per cent.; red cells, 4,620,000; white cells, 12,000. Forty-eight hours after ether: Hæmoglobin, 80 per cent.; red cells, 5,700,000; white cells, 10,600. At this time there was a decided increase in the number of small lymphocytes, yet the polymorphonuclear cells formed the greater portion of the leucocytes. Few myelocytes were present. The erythrocytes were apparently normal. Seventy-two hours after ether: Hæmoglobin, 86 per cent.; red cells, 4,780,000; white cells, 7400. On one side of the smears three myelocytes were found, otherwise a stained specimen appeared to be normal.

Experiment V. Animal used for Experiment II. was again etherized May 2, 1902 (seventeen days after the first anæsthesia). Animal now in apparently perfect health. Ether (Squibb's) was given for one hour and forty-five minutes. Blood examinations were made immediately before ether, and after the animal had been anæsthetized for one hour, and for one hour and forty-five minutes, respectively; also twenty-four hours and forty-eight hours after the anæsthetic had been withdrawn.

Before ether: Red cells, 3,016,600; white cells, 8000; hæmoglobin, 50 per cent. Stained specimens appeared as normal. One hour after ether: Red cells, 5,120,000; white cells, 12,000; hæmoglobin, 49 per cent. Slight poikilocytosis. One and three-fourths hours after ether: Red cells, 4,440,000; white cells, 13,600; hæmoglobin,

43 per cent. Total quantity of ether employed, 9 drachms. Red cells show great variation in both size, form, and staining properties of the erythrocytes. Cells staining but feebly are common, and usually these are distorted. Leucocytes appear to be normal as to varieties. Twenty-four hours after ether: Red cells, 3,820,000; white cells, 8000; hæmoglobin, 53 per cent. Crenated cells common, otherwise normal. Subsequent examinations revealed similar findings.

Second etherization of Animal III.

EXPERIMENT VI. Eleven days after first ether. Before ether was given, red cells, 4,730,000; white cells, 8000; hæmoglobin, 79 per cent. Stained specimens appear normal. Ether for twenty minutes, giving all the animal could take, hæmoglobin, 57 per cent.; red cells, 7,880,000; white cells, 8000; died five minutes later. Stained specimens showed great variation in the size of the red cells. All the red cells were extremely pale and poor in hæmoglobin except a few microcytes. Many crenated cells and poikilocytes were found. Microcytes were common and macrocytes numerous. Few nucleated reds (normoblasts) were also observed.

It is of interest in this connection to note, as shown by Experiment V., that during a second etherization, seventeen days after the first, the changes in the blood were less pronounced than at the first; also that this loss of hæmoglobin is restored in from twenty-four to forty-eight hours following the anæsthetic. Again, the duration of the anæsthetic state does not appear to influence materially the blood findings.

These few laboratory experiments show clearly that the fall in the color index in primary anæsthesia reaches its lowest level about twenty-four hours after the anæsthetic state is over; also that one-half of this fall takes place during the first hour after anæsthesia, the other half during the succeeding twenty-three hours. The blood regeneration goes on quite rapidly following the anæsthetic condition, but the hæmoglobin is restored more slowly than the erythrocytes; hence the cells are inadequately supplied with hæmoglobin. At the end of twenty-four hours the color index begins to rise rapidly, and it reaches the normal level after the lapse, approximately, of seventy-two hours in man. A few myelocytes, however, were still present at this time.

The polycythæmia noted does not depend solely upon the preparatory treatment, including purgation, since this was purposely omitted in some of the above cases (Case IV.). The decidedly increased blood production immediately following the administration of the anæsthesia would appear to be a factor in bringing about the polycythæmia according to our experiments. It seems to me that the suddenness with which a rather extensive blood destruction takes place during etherization accounts in a satisfactory manner for the occasional occurrence of polycholia, since there occurs an equally rapid liberation of hæmoglobin which, if acted upon by the hepatic cells, must result in an increased

amount of bile pigment. Of course, a mixed etiology may obtain in some cases.

Case II. *Intense Jaundice in Connection with Lobar Pneumonia.*—C. E. V., aged fifty-three years; married; occupation, clerk; first came under my observation March 4, 1901. The family history showed the ancestors to have been unusually free from hereditary taint, except possibly slight traces of gout and hepatic torpidity in the father. The patient had no recollection of having had any disease of childhood, with the exception of measles. Social habits unexemplary; for many years he had suffered from alcoholic inebriety, and more recently had shown symptoms indicative of the early stage of hepatic cirrhosis. Analogous changes were believed to be present in the kidneys, as suggested by the urinary findings. Moreover, at the age of about forty years he contracted syphilis, and the changes in the liver were ascribed, in part at least, to the syphilitic infection. About three years prior to his death the patient had had pneumonia.

For several months previous to his last (fatal) illness the craving for alcohol seemed to be continuous and resistless; it was accompanied by an unusual degree of exposure to wet and low temperature. The last illness began as an influenza, lasting four days, when pneumonia affecting the lower lobe of the right lung set in without the usual ushering-in rigor and other severe invasion symptoms.

During the preliminary or influenza stage the temperature ranged from 99° F. to 101° F., and with the onset of the pneumonia it rose to 103° F., and finally to 104° F. The temperature curve was of irregularly continued type. The respirations varied in rate from 40 to 60 per minute, and the pulse continued to be regular, of fair volume and force until two days prior to death, when it grew quite rapid, compressible, and arrhythmic. Prune-juice expectoration was present. At the end of the seventh or eighth day of the illness signs of consolidation affecting the left base were also in evidence.

Jaundice of moderate intensity developed on the second day of the pneumonia and gradually deepened until it became intense; this was shortly before the fatal termination occurred. The stools were at no time infrequent, and always contained some bile pigment. During the last four days of life the dejecta numbered from four to six daily, and near the close were passed involuntarily. The urine contained bile pigment in abundance, a small percentage of albumin and tube casts, principally of the granular variety.

With reference to the bile pigment, it may be further stated that it appeared to continue to increase in amount as shown by the color of the urine, reaching its highest limit at the time of death, as was stated respecting the icteric discoloration of the bodily surface and conjunctivæ. Death was preceded by marked nervous disturbances—active delirium—signs of intense motor irritation, as shown by subsultus and coarse tremors. On account of the urinary findings, the nervous phenomena were ascribed in part to uræmia. Delirium tremens did not, as had been feared, carry off the patient.

Autopsy, twenty-four hours after death, by Dr. L. Napoleon Boston: Well-nourished male, apparently fifty years of age; everywhere the

skin was jaundiced to an extreme degree. There were also many small cutaneous hemorrhages over the chest and abdomen; the superficial veins of the abdomen were enlarged; there was a small umbilical hernia and slight œdema of the hands, feet, and ankles. The percussion note became dull over the right lung at the third interspace, extending downward to a point two inches below the costal margin. The left lung showed slight impairment of the percussion note at the base; only a small incision into the abdomen was allowed. Abdominal fat three inches in thickness; abdominal cavity contained some fluid (removed by undertaker). Viscera including the liver were jaundiced; the stomach showed slight congestion, probably post-mortem.

Duodenum showed no evidence of congestion at any point. The mouth of the ductus communis was in no way obstructed. Upon pressure over the gall-bladder bile escaped into the duodenum. The gall-bladder and ducts presented nothing abnormal on macroscopic examination. The edges of the liver were nodular, and at many points there were decided contractures—attempts at the formation of additional lobes. On the superior surface, near the junction of the right and left lobes, it was decidedly nodular (hobnail). Each of the small liver lobules stood out clearly and was surrounded by a rather broad band of yellowish tissue, which was depressed. The base of the right lung was consolidated, as was also a small portion of the left lung posteriorly. At several places the organ had been entered by the needle and injected with the embalming fluid. The kidneys were not examined for the reason that it was not permitted.

The report of the microscopic findings in the liver by Prof. Coplin was as follows:

The changes were those typical of fatty cirrhosis, with marked cholangitis affecting the intrahepatic excretory ducts. Extensive desquamation of biliary epithelium was observed, and the presence in the smaller bile ducts of bacteria resembling the colon bacilli.

Such cases as the above prove with complete certainty that in some instances of pneumonic jaundice, at least in which there is no obvious macroscopic obstruction to account for the symptom, the microscopic examination may reveal the changes of a cholangitis. J. E. Graham[8] affirms that the jaundice of cardiac insufficiency and of pneumonia is accounted for by the fact that the bile is secreted under low pressure, so that the changes in the circulation may cause it to flow from the cells into the veins rather than into the biliary radicals. Is it not a fact, however, that bile is ordinarily secreted under low pressure? According to certain observers it is of toxic origin, while still others believe it to be due to catarrhal lesions affecting the duodenum and larger excretory ducts of the liver. In the case reported above, the intrahepatic cholangitis was doubtless the active causative factor. May not the increased amount of bile pigment have set up an inflammation of the fine biliary ducts? The obstruction to the outflow could not have been complete, owing to the constant presence of biliary color-

ing matter in the dejecta. Hence, the toxic element may also have played no inconspicuous part in the causation of the jaundice. The *modus operandi* would be similar to that pointed out in connection with Case I. I have seen two additional cases in which the lesions of an ordinary catarrhal jaundice existed, hence the icteric tint may at times be solely dependent upon the latter changes.

Mallory[9] and Longridge[10] have called attention to foci of necrosis, which they claim are common to the acute infections, including lobar pneumonia. It is of two varieties, central or diffuse, and focal. In the former (central) the lesion begins in the centre of the lobules and spreads peripherally. Focal necrosis may rarely be due to the toxin of pneumonia. Neither form of necrosis, however, was found on histological examination of the liver from my case.

In 1898, Türck[11] showed that when the pneumonic infection is severe, or the patient has low vitality, nucleated red cells, principally normoblasts, and in a lesser degree also megaloblasts appear in the peripheral blood. Maragliano has observed "degenerative" changes in the red cells in severe cases. It is interesting to note that in the observations upon the effect of the anæsthetic (ether) on the blood of our rabbits, an increased number of nucleated red cells, mostly normoblasts, and other degenerative changes were observed. The point is that increased hæmolysis from any cause may induce similar blood changes, and may also be the cause, with the aid of the liver function, of a symptomatic jaundice, as before explained. Again, when the liver is the seat of chronic pathological change, as in the case just reported, the obstruction to the outflow of inspissated and abnormally viscid bile is far greater than in a previously normal organ.

In this connection I desire to direct attention to the question of the causes of death in this and similar cases. It is doubtless true of obstructive jaundice that death is, in the majority of cases, due to the underlying condition that induces the jaundice rather than to the icterus itself. In some cases, however, and more especially those in which an excess of bile pigment is generated, the poisonous effects of the latter may prove fatal. Bouchard regards the biliverdin as the toxic constituent. As clinicians we are not so much concerned with the question of the special ingredient of the biliary secretion that possesses the poisonous properties—a moot point—as with the fact that a serious and even fatal condition (so-called cholæmia) may be suddenly induced by this secretion.

Just how death is brought about from the poisonous action of the bile is imperfectly understood. Much depends upon the previous condition of the kidneys. Moreover, I am firmly of the opinion, based on personal observation, that an acute nephritis is often set up by the bile pigment in the process of elimination through a normal urinary

tract. This fact is corroborated by Case V. of my present series (*vide infra*).

It is rare, indeed, to meet with jaundice during the secondary stage of syphilis. Through the kindness of my friend and assistant, Dr. Boston, I am able, however, to present brief notes of an illustrative case:

CASE III.—M. C. D., aged nineteen years; American; prostitute; first came under observation June 10, 1897. Parents and four brothers living and fairly healthy; all, however, are alcoholics.

Past History. She had some of the affections of childhood, afterward continued in good health until six or eight weeks ago, when she developed an eruption, the remains of which show it to have belonged to secondary syphilis. The patient has no knowledge of an initial sore. Three weeks ago she noticed a swelling of the feet and abdomen, at the same time developing a yellow vaginal discharge. A pelvic examination showed a cervical discharge and a cervix that was ulcerated and bleeding. The conjunctivæ and skin were markedly jaundiced, and the feet swollen to twice their normal size. The heart sounds were weak, valvular, and distant, but fairly regular; the liver was enlarged and tender to pressure; otherwise the physical signs were negative.

June 22, 1897. There is a wave of fluctuation over the abdomen; temperature, 101°; pulse, 120; respiration, 24. The patient complained of pain in the region of the liver and at angle of scapula; abdomen much distended.

23*d*. The condition as noted yesterday, except temperature, now 102°, and respiration 30 and difficult; she sits pillowed up in bed; pain severe, and size of abdomen increasing. Lips and tongue fissured, the former bleeding; also oozing of blood from the nose and gums; slight systolic murmur at apex; vomited twice during the day; face distinctly puffy; intense jaundice.

Examination of Urine. Specimen porter color, specific gravity 1020; sediment heavy; reaction acid. Chemically it was found to contain considerable albumin and bile pigment, but no sugar. The microscope revealed bile-stained pus, tube casts (granular and epithelial), and epithelium (vaginal and vesical).

June 24*th*. On the following day the patient greatly improved both locally and generally, although vomits a dark coffee-colored material every few hours.

26*th*. Jaundice still marked; stomach non-retentive, all food and dark-colored fluid vomited; an examination of stools showed bile pigment, epithelium, etc., but no pus.

27*th*. Pain persists in abdomen, but there is no vomiting, and the jaundice is disappearing. At no time was there an absence of bile pigment from the stools. The patient now improved day by day under anti-syphilitic treatment, until at the end of four to five weeks all symptoms had vanished.

The cause of the jaundice in this instance was believed by Dr. E. P. Martin, who saw the patient by request, to be perihepatitis. According to White and Martin,[12] jaundice developing during the secondary period is rarely due to syphilis. The great majority of such cases,

when unattended by hepatic enlargement, as in the case herewith reported, are caused by intercurrent affections, such as a catarrhal condition of the bile ducts, "and are neither directly nor indirectly dependent upon constitutional syphilis." It is not likely that a gumma in the portal fissure was the cause of the jaundice in this case, as it had not progressed beyond the second stage. While the jaundice in this case was ascribed to the perihepatitis, although no blood examination was made, it is to be recollected that the syphilitic virus may cause extensive dissolution of the erythrocytes and marked oligochromæmia in the second stage of the affection. In this stage all forms of nucleated reds and poikilocytosis have also been commonly met with, especially when, as in this instance, the patients have belonged to the semi-starved, pauper element of society. The blood changes are identical with those characterizing toxæmic jaundice, and they may sustain an indirect causative relation to syphilitic icterus.

The question as to the cause of the fever in this case is an interesting one. Was it occasioned by acute nephritis? or by an intercurrent cholecystitis? or, finally, was it an instance of syphilitic fever? According to the results of the therapeutic tests, it was almost certainly ascribable to syphilis. Janeway[13] and others have reported cases in which fever attended the late manifestations of syphilis. It also occurs in the second stage. I have recently met with a case in a male, aged twenty-five years; it lasted about two weeks, and on several occasions the temperature rose to 102° F. Basset-Smith[14] reports a case in which a mis-diagnosis of malaria had been made on account of an intermittent fever curve. As the nephritic symptoms inducing dropsy disappeared under syphilitic treatment, they were doubtless of syphilitic origin. Allaria[15] also invites attention to early (secondary) syphilitic nephritis, with severe albuminuria, anasarca, and recovery under specific treatment.

Case IV. *Jaundice due to an intercurrent acute inflammatory condition in the course of hepatic cirrhosis.*—T. O. D., aged forty-four years; occupation plumber; single; admitted to the male medical wards of the Medico-Chirurgical Hospital, March 20, 1902. The family history is perfectly good, except that one sister died at the age of twenty-three years of some unknown cause. The patient had had none of the affections of childhood. Two attacks of acute articular rheumatism, the first at thirty years of age, lasting fourteen weeks, and the second at forty-one years, duration five weeks. During convalescence from the last attack of rheumatism, he drank heavily and steadily for a year or more, when he developed evidence of chronic nephritis, including dropsy of the feet and legs. He then abandoned alcohol, was placed upon appropriate treatment, and apparently recovered.

Shortly thereafter, or ten months ago, he had an attack of pneumonia, for which he was treated in the Medico-Chirurgical Hospital. Following this illness he again became intemperate, using whiskey in

excess; this he continued until date of admission. The illness that led him to apply for relief began six weeks previously, with indefinite symptoms, as fatigue, anorexia, constipation, and other prodromata of liver cirrhosis.

On March 19th (one day prior to admission) he developed intense pain in the region of the gall-bladder, radiating to the right shoulder, abdomen, and back. Fever developed; it was of irregularly continued type, and did not range high, the maximum temperature not exceeding 105.3° F. There were no rigors; the pulse was moderately accelerated (not slowed). The urine analysis at this time showed the presence of bile pigment, a small percentage of albumin and fine granular and epithelial casts. A physical examination indicated great enlargement of the liver, the lower border reaching to a line one inch below the umbilicus. The gall-bladder area was tender to the touch, but this viscus was not palpable. The second urine analysis, made March 25th, yielded results similar to those of the first, although the albumin was increased in amount to about 1 per cent. The skin was now a deep saffron hue. Fever more marked; patient quite delirious at night, exhibits noisy respiration, and is profoundly prostrated.

March 26th. All symptoms, including the jaundice rapidly abating; the liver is also diminishing in size. Albumoses searched for, but not found at any of the urinary examinations. The stools were not clay-colored, indicating no obstruction in the excretory ducts. This remission in the symptoms lasted a few days and then they reappeared, although less marked. (See Chart 2.)

31*st.* The jaundice returned with the recurrence of the fever.

April 17th. The temperature has been ranging near to the normal grade for one week, and the jaundice almost entirely vanished.

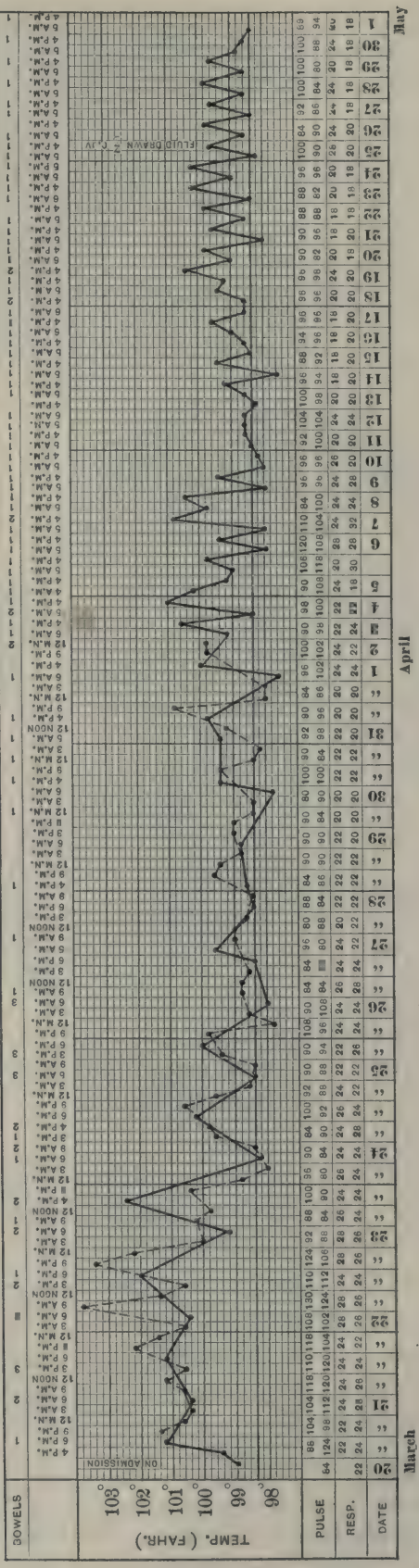
May 1st. The temperature has become nearly normal after a slight rise about ten days ago, and the patient has been growing stronger. Ascites has developed acutely during the past month; abdomen was tapped this day and 108 ounces of bile-stained fluid removed. A subsequent physical examination indicated only moderate hepatic enlargement, the organ having rapidly diminished in size during the previous two weeks. Very slight jaundice remained.

9th. Slowly improving. A blood examination resulted as follows: Reds, 3,790,000; whites, 9000; hæmoglobin, 55. Cells of normal size and form.

That cirrhosis may often be due to multiple causes is universally conceded. Again, many cases have as their principal etiological agent an infecting microbe. Thus tuberculosis, syphilis, malaria, one and all, may cause it. It is more particularly in the hypertrophic form of the disease that the etiology is often obscure. The case I have here reported is to be classed as alcoholic cirrhosis, according to the clear history. It is not unlikely, however, that as regards many cases of this variety of atrophic cirrhosis, our notions concerning etiology may be upset by future investigations.

Adami[16] affirms that in cattle the infective disease known as "Pictou disease" presents hepatic changes similar to those found in cirrhosis in man. The irritant in this case is believed to be a bacteriological toxin,

CHART 2.


BOWELS
TEMP. (FAHR.)
103°
102°
101°
100°
99°
98°
ON ADMISSION
FLUID DRAWN 2° C. IV
PULSE
RESP.
DATE
March
April
May

which acts as a protoplasmic poison. Hektoen[17] reports a case of cirrhosis of the liver in animals, produced by a member of the colon group, and another that was caused by inoculation of the bacillus which belongs to the pseudodiphtheria group. Cultures were made from the bile-stained peritoneal fluid withdrawn in my case, with the following result: Bouillon cultures at twenty-four hours showed an abundant growth of motile bacilli, which on staining and further study were found to be members of the colon group. No other organisms were present in cultures. Slides were smeared with the peritoneal fluid, and when stained were found to show few bacilli which decolorized by Gram's method. No tubercle bacilli were found. The fluid was lemon-yellow in color, turbid, and presented a flocculent sediment; its specific gravity was 1010, reaction slightly alkaline, and contained about 0.12 per cent. of albumin.

This case also represents a group or class of cases that are by no means uncommon, and in which chronic hepatic disease, most commonly cirrhosis, is suddenly complicated with an acute inflammatory condition. In Case IV., just related, the intercurrent affection was regarded as being cholecystitis.

The principal features in this instance were similar to those of Weil's disease, namely, jaundice, fever, and albuminuria with casts. Rigors were absent, however, and the temperature curve closely resembled that of relapsing fever, as may be seen from a glance at the accompanying fever chart. (See Chart 2.) The intensity of the jaundice also corresponded pretty closely with the degree of elevation of temperature. This so-called relapsing jaundice must, it seems to me, be due to an infection and re-infection, but whether or not the colon bacillus is to be incriminated is still uncertain. Karlinski and others have described an epidemic jaundice of unknown etiology, in which the febrile movement pursued a similar course. These facts tend to prove the infectious nature of the condition, but it may be of varied etiology. H. Neuman[18] goes so far as to state that there is no demonstrable difference between epidemic infectious jaundice and simple catarrhal jaundice, which, he holds, is also due to an infection.

Case V. *Mixed cirrhosis, biliary and atrophic variety.*—This patient was under the charge of Dr. I. Newton Snively, to whom I am indebted for the notes of the case.

Mr. H. F., aged twenty-eight years; American; weight about 240 pounds; height 5 feet 10 inches; book-keeper by occupation. The family history is good, except that the father had been afflicted many years with epilepsy, and died from apoplexy.

Previous History. He had the ordinary diseases of childhood; measles, mumps, chicken-pox, and whooping-cough. As a boy he complained unusually of shortness of breath upon exertion, such as running and jumping, etc. He has been drinking quite heavily since he was nine-

teen years of age, and for two years and a half past has taken whiskey in enormous quantities, perhaps from a quart to a quart and a half every twenty-four hours; yet was never intoxicated so as to be unable to attend to his duties as book-keeper, etc.

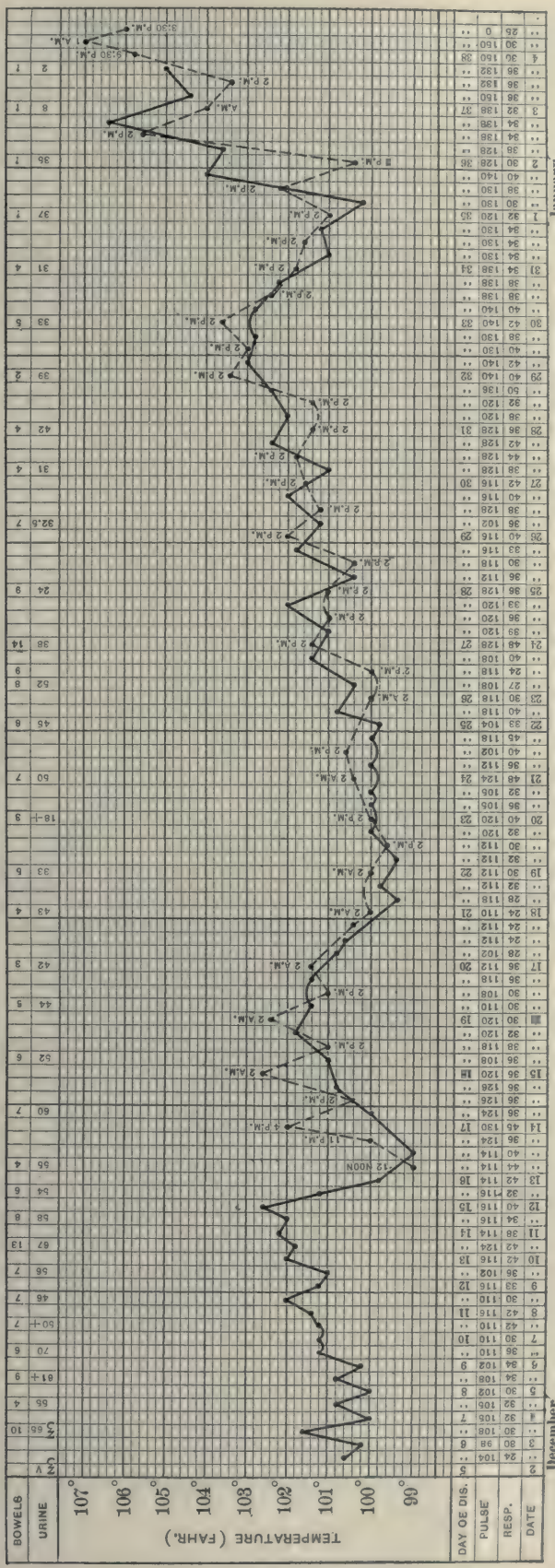
About July, 1900, he noticed a sore on the right upper thigh about two inches back of the scrotum ; he attributed it to chafing, but as it refused to heal, he consulted Dr. Clifford Scott, who suspected specific infection, treated him accordingly, and in three or four weeks the sore healed. The patient was an inveterate smoker of cigarettes. Since twenty-one years of age he has been growing stouter, and for two years past has been extremely corpulent—in fact, almost helpless at times. One year before the onset of his present sickness he noticed a dropsical condition of the lower limbs, which later involved the scrotum, and he suffered greatly with shortness of breath, especially upon exertion. He was obliged to sleep propped up with head-rest and pillows for several months. His appetite, however, was enormous, and he ate largely of all kinds of food until the beginning of the present sickness.

The above symptoms, œdema of the lower limbs and scrotum, shortness of breath on exertion, etc., grew gradually worse until on November 29, 1901, he was compelled to stay in his room. At this time the abdomen was enormously enlarged, the limbs and scrotum were swollen to their utmost capacity and were oozing fluid. His pulse and respirations were rapid, as shown by the chart. He was tapped in the abdomen and scrotum a number of times; also the limbs.

Physical exploration, after paracentesis, by palpation and percussion showed an enormously enlarged liver. I saw the patient several times in consultation with Dr. Snively at intervals of several days. During the last month of life the temperature ranged from 99° to 102.3° F., ending with hyperpyrexia (see Chart 3); this was accompanied by delirium, prostration, and other evidences of an acute infection, without our being able to recognize the nature of the morbid process. The skin and conjunctivæ had been jaundiced for about three weeks before death. The tappings show that up to December 7, 1901, 384 ounces of fluid had been drawn off; also estimated 64 ounces on December 8th, which simply represented the oozing from scrotal openings made by the trocar and the oozings from the legs where the trocar had been used. The charts show several later tappings. Urinary analysis showed no sugar, albumin, or casts, except during the last four or five days of his life, when the urinary findings characterizing acute nephritis developed. He died January 4, 1902.

Post-mortem findings twenty-four hours after death by Dr. L. Napoleon Boston : Body of a male, large in stature, face swollen, and skin and conjunctivæ jaundiced. The veins over the abdomen and chest were dilated. A dull percussion note on the right side, commencing three inches above nipple and extending to crest of ilium. On opening the chest 100 c.c. of bloody fluid was found in each pleural sac; right lung pushed up to third rib and the arch of the diaphragm lifted to the same point in nipple line. Hypostatic congestion rather extensive in the left lung, and confined to the base of right lung. The myocardium was contracted, its walls thin, and showed fatty changes on section; the chambers were occupied by dense fibrous clots. Microscopic study of the heart muscle impossible, owing to the embalming fluid. The stomach was normal except that its walls were slightly congested,

CHART 3.


TEMPERATURE (FAHR.)
107° 106° 105° 104° 103° 102° 101° 100° 99°
BOWELS
URINE
DAY OF DIS.
PULSE
RESP.
DATE
December
January
12 NOON
11 P.M.
4 P.M.
2 P.M.
2 A.M.
3 P.M.
3:30 P.M.
1 A.M.

but the ductus communis choledochus was patulous, and a needle could be passed directly into the gall-blader. The gall-bladder was normal and contained about one-half ounce of bile.

Liver. Weight 6040 grammes; color a greenish-yellow, surface smooth, slightly mottled, capsule free, and edges rounded. On section, resistance to the knife was increased; the surface presented a rather granular aspect; the acini were uniformly prominent, elevated, and each surrounded by a band of yellowish-white tissue, which showed slight depression. The needle of the embalming trocar had pierced the organ at several points, hence attempts at section for microscopic study were not altogether satisfactory, although the appearances were in the main those of fatty cirrhosis of the organ. The liver tissue was everywhere clearly and distinctly bile-stained. The kidneys presented the usual naked-eye appearance of acute nephritis, and this was also shown by microscopic study.

A microscopic examination of the liver by Dr. Coplin revealed the following:

"There is a large amount of elastica, which is intralobular and interlobular; enters lobules and often surrounds columns of cells, and at points is increased around smaller bile ducts, and is still more increased around the larger biliary branches. Newly-formed tissue between lobules, which is, for the most part, young and fully formed; fibrous tissue is not so abundant as the gross specimen would have led one to believe. The liver cells show fragmentation of protoplasm and nuclei, and advanced granular degeneration is evident in many cells. Young cell deposits are present, even within the lobules. Uniform fatty infiltration is fairly evenly distributed throughout sections.

"Epithelium of bile ducts is advancedly granular, often fragmented, and often desquamating. Evidence (distinct) of new bile duct formation is wanting. Many of the lobules show intense bile-staining, more pronounced at periphery than at centres. The lobules showing less fatty infiltration, least fragmentation of cells, and least young cell invasion and increase of elastica, are most stained with bile (and are probably secreting bile). Many stained cells are shrunken. Mixed cirrhosis, biliary, and fatty alcoholic varieties."

The features of greatest clinical interest in this case are the intense jaundice, the fever, and the acute nephritis coming on in the course of cirrhosis. A glance at the temperature chart will show that hyperpyrexia, with tendency to daily increase of fever, supervened two days before the occurrence of the fatal termination. The curve also shows a disposition, though incomplete, to relapsing febrile jaundice. Bradycardia was not present at any time; on the other hand, the pulse was accelerated throughout, and during the last three weeks of life much increased in frequency. The post-mortem failed to reveal any localized inflammatory or other lesions, save those of the liver and kidneys, to account for the fever, and it should be recalled that the urinary findings were negative up to within a week of the fatal termination. It seems to have been an instance of febrile jaundice arising in the course

of hepatic cirrhosis with the secondary development of acute nephritis. The case bears out the view previously expressed, namely, that febrile, infectious jaundice may be complicated with nephritis, and the latter condition may result from irritation of the renal tissue by the bile pigment in the process of elimination from the system. It is to be borne in mind, however, that in many of the acute infections nephritis due to the local irritant effect of the special toxin is not very uncommon. Uræmic symptoms attended near the close in Case V.

In conclusion, while the cases reported above do not furnish a basis for definite, conclusive inferences, they suggest a few queries and propositions:

1. Is there a true polycholia due to the conversion into bile pigment of the hæmoglobin that is suddenly liberated by certain poisons, as ether, chloroform, and the like, or the toxins of the acute infections, as, for example, lobar pneumonia?

2. Doubtless other causative agents are often operative in cases that fall under 1.

3. As there could be no jaundice without the presence of the liver, the term "hematogenous" is misleading, and should be regarded as obsolete; the term "toxæmic jaundice" may be, however, appropriately applied to the cases of "hepatogenous" icterus, in which the blood changes are a more or less striking pathological feature.

4. May not the jaundice rarely seen in secondary syphilis be toxic in nature, at times at least, rather than purely "hepatogenous?"

5. Admitting that there are well-established causes for the hepatic cirrhosis, more particularly of the atrophic form, the etiology is but imperfectly understood.

6. Clear evidence to show that the hepatic cirrhoses are, in many cases at least, of microbic origin is accumulating.

7. The intercurrent acute inflammatory conditions with jaundice in the course of cirrhosis of the liver are doubtless micro-organismal in nature. (See Cases II., IV., V.)

8. Relapsing febrile jaundice is also to be classified as an infection; it will probably be shown on further investigation to be due to a member of the colon group. (See Case IV.)

9. It is probable that the jaundice of hepatic cirrhosis is, in a certain sense at least, toxic in nature.

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ABSCESSES OF THE LIVER FOLLOWING TYPHOID FEVER.

By John G. Sheldon, M.D.,
of telluride, col.

John H., aged thirty-four years, came to me June 24, 1901, complaining of pain in the right side; chilly feelings and sweats, and great weakness. He said that three days before he saw me he had left his bed, where he had been confined for six weeks suffering from a disease diagnosed by his attending physician as typhoid fever. The history of this illness was typical for an ordinary case of typhoid fever, except that he felt that he was regaining strength very slowly, and that he had felt a heaviness and dull pain in the right side during the last week that he remained in bed.

The patient's previous history was negative. He suffered from measles when a child, and had smallpox when twenty years of age, but had had no other illness.

The examination showed a well-developed, poorly-nourished and emaciated middle-aged man. His skin seemed somewhat darker than normal, but he was not jaundiced. The mucous membrane of the lips and conjunctivæ was pale. There was marked tenderness in the region of the liver, and I inferred from the physical findings that the liver was diffusely enlarged. Its lower border was well defined and extended a hand's breadth below the costal arch at the outer border of the right rectus muscle. The upper border of relative hepatic dulness extended, in the right mammillary line, to the upper border of the third rib. Examination of the chest showed diminished expansion and respiratory excursion on the right side. The apex of the left lung seemed duller than normal. Harsh breathing was found in the apex of the left lung and over the lower portion of the right. A few moist râles were present in both lungs posteriorly. No friction rubs were heard. The heart was slightly enlarged transversely, and a systolic murmur was present over the pulmonic area. No thrills were found. The pulse was beating 108 times per minute; was not strong, but was regular. The temperature was 101° F. The spleen was not felt. There was no tenderness in the lower abdominal region; and no evidences of fluid in the peritoneal cavity could be found. The remainder of the examination was negative. The urine showed a trace of albumin, but was otherwise normal.

A diagnosis was not made at this time. A diagnosis of cardiac insufficiency, with passive congestion of the liver, was not warranted.

Tuberculosis and syphilis could not be positively excluded, but the symptoms led us to suspect the presence of an inflammatory condition in the liver.

The developments in the case were as follows:

June 25th. Chill in the evening, followed by sweating. Temperature, 102° F.; pulse, 120. Pain in right side severe. Blood examined for malarial organisms—none found.

26th. Morning temperature 99° F. Slight chill at 2 P.M. Temperature, 8 P.M., 100° F.; pain continuous; tenderness marked.

27th. Leucocyte count, 18,000; differential count not made. No tubercle bacilli found in the sputum.

The patient remained about the same during June 28th, 29th, and 30th. His symptoms were gradually increasing in severity, and his liver was becoming larger. Several punctures were made into the right hepatic lobe from behind, and on the evening of June 30th I introduced a needle between the eighth and ninth ribs about three inches from the spine, and at a depth of five inches, withdrew about a drachm of thick, yellow pus.

Owing to the marked enlargement of the liver anteriorly and to the absence of signs of pleural adhesions, I decided to attack the liver from in front, and on July 1st an incision, three inches long, was made parallel to the right costal margin, the centre of the incision corresponding to the outer border of the right rectus muscle. The liver was smooth, and many small yellow areas were seen on its surface. No adhesions between the peritoneum and liver were observed. The peritoneal cavity was protected with gauze, after which an aspirating needle was introduced into the liver and pus found at the depth of about one inch. This abscess was opened with a blunt artery forceps and contained about a drachm of pus. Another abscess was located to the right of the first and was drained through the same opening. The bleeding became free, but was easily controlled by a pack or by introducing the finger into the liver wound. By using the needle, uterine probe, artery forceps, and finger, I located and drained five abscesses, none of which contained more than two drachms of pus. I then introduced a rubber tube, wrapped the gauze into the wound, and packed the lumen of the tube to prevent hemorrhage. The anæsthetic which consisted of $\frac{1}{100}$ of a grain of hyoscine hydrobromate, and $\frac{1}{4}$ of a grain of morphine hypodermically, followed in one-half hour by ether, was taken nicely, and the operation, which was of short duration, was not attended with much shock.

The patient slept five or six hours after the operation, after which I removed the pack from the lumen of the tube. A considerable amount of pus and bile, with some blood, escaped. Eight hours after the operation the patient's temperature was 100° F., his pulse 106. He had very little pain—less than before the operation—and said that he felt relieved. For one week the drainage was profuse, and the liver diminished markedly in size. The temperature rarely came down to normal, but the pulse remained good, and very little pain was complained of. The tube was removed on the sixth day following the operation and a gauze drain substituted. On July 10th the patient had a chill; his pulse was 118; temperature, 102° F., and he complained of considerable pain in the right side. Examination showed no changes in the physical findings—the liver dulness extended, pos-

teriorly, as high as the eighth rib. A uterine probe was introduced deeply into the liver wound and a small amount of pus was discharged. This did not give the patient relief. The chills and fever recurred and the pain continued, being situated more posteriorly than usual.

On July 16th the liver flatness extended to the lower border of the scapula. The anterior margin of the liver was found to be about one finger's breadth below the costal arch. There was no respiratory excursion on the right side. Under local anæsthesia a section of the ninth rib was removed in the posterior axillary line. The pleura was opened and not found adherent to the diaphragm. Twelve hours later pus was located at a depth of two inches from the base of the wound, and a large abscess cavity was opened by using a blunt artery forceps. A drainage tube was inserted. The patient felt relieved, the chills ceased, and the temperature and pulse became better. The patient at this time was very weak and somewhat emaciated. He got along very comfortably until August 1st, when he developed a cough. Pus still continued to discharge through the operation wound—the tube having been removed. From August 1st to August 10th the patient gradually failed. The pulse was weak and beat from 110 to 130 times per minute. The temperature was irregular, ranging from 100° to 101° F. No decided chills were complained of. The cough became more severe, and on August 8th blood was expectorated. On August 9th the patient complained of difficulty in breathing. On August 10th the dulness had extended higher on the right side than it had been previously. No movable dulness was made out. I introduced an artery forceps into the wound and opened the pleural cavity in an upward direction. The opening was dilated and a tube inserted. The improvement following this procedure was slight. On August 15th I explored the pleural cavity with the finger, broke up some adhesions and liberated a considerable amount of pus. The patient failed gradually. On August 20th he developed a diarrhœa, which lasted until August 22d, when he died.

The autopsy was done August 23d. The external examination of the body was negative, except for the presence of the two operation wounds. No icterus present.

The peritoneal cavity contained a small amount of clear, straw-colored fluid. The peritoneal surfaces were everywhere smooth, except that there were a few adhesions over the right lobe of the liver.

The pericardium contained a small quantity of clear fluid. Its surfaces were everywhere smooth. The heart was small, weighed 225 grammes. The myocardium was pale and friable. The cardiac valves were normal.

Many adhesions and a small quantity of pus were found in the right pleural cavity. The apices of both lungs were adherent. The lower portion of the left pleural cavity was normal. The pleura on the right side was markedly thickened.

The lower lobes of both lungs were hyperæmic, especially in the posterior parts. In the apex of the right lung several irregular cicatrices were found. A small cavity and a few scars were found in the apex of the left lung. The middle lobe of the right lung was firm and cut with resistance. Muco-pus could be squeezed from the bronchi. The bronchial glands were slightly pigmented. Calcareous deposits were found in two of them. There was found an opening in the diaphragm

—large enough to admit the index finger—which communicated with a cavity in the right hepatic lobe.

The liver weighed 1650 grammes. The right lobe presented a cicatrix and an irregular depression over its anterior surface. The posterior part of the right lobe was adherent to the diaphragm. On section the right lobe showed many irregular cicatrices in its anterior part. Situated in the posterior part of the right lobe of the liver was a globular cavity, 7 centimetres in diameter, communicating with the right pleural cavity through an opening in the diaphragm. This cavity contained dark-colored pus. It had no definite lining membrane. The liver tissue surrounding the abscess cavity was hyperæmic and friable.

The left hepatic lobe was enlarged in proportion to the size of the right. On its inferior surface five globular abscess cavities could be seen. These abscesses measured from 2 to 4 centimetres in diameter, and projected from the surface of the liver. On section the left lobe contained many abscesses, most of which were small. All of them had a definite lining membrane; and all of the smaller ones could be found to communicate directly with a branch of the portal vein. Pus could be squeezed from most of the portal vein radicals.

The biliary apparatus seemed normal; as did the hepatic artery. The splenic, portal, and superior mesenteric veins showed no gross abnormal lesions.

The lining of the small intestine was hyperæmic. No ulceration was found. Two Peyer's patches near the ileocæcal valve were elevated and indurated. The remainder of the patches presented a shaven-beard appearance. The serosa of the small intestines was normal. The mucosa of the large bowel was hyperæmic. Otherwise, the large intestines were normal.

The appendix showed no abnormal changes. The mesenteric glands were enlarged and indurated. Softening was found in the interior of one gland, 2 centimetres in diameter.

The kidneys were slightly larger than normal. Their capsules were not adherent. On section they were granular and friable, but otherwise they presented nothing abnormal. The remainder of the examination revealed nothing of interest. The nervous system was not examined.

The succession of pathological changes leading to the patient's death were believed to be as follows:

Typhoid fever; carrying of infectious material from the intestines or mesenteric glands by the portal vein to the liver; suppurative pylephlebitis, with abscess formation. The injury to the liver tissue done at the first operation resulted in the formation of a large abscess, differing from the smaller abscesses by being surrounded by a zone of hyperæmic liver tissue, and by being destitute of a definite lining membrane. This abscess might be classed as a secondary pyosepticæmic abscess, as described by Andrew Davidson.[1] The empyema resulted from the second operation.

The diagnosis of typhoid fever was made from the clinical history and from the post-mortem findings in the intestines. A Widal reaction

was not tried. Slides made from the first operation and from the small abscesses found in the left hepatic lobe on post-mortem examination showed the presence of a small bacillus, which might have been either the typhoid or the colon bacillus. However, typhoid fever seems the most probable cause for the patient's primary sickness.

The belief that the hepatic abscesses resulted from diseased portal vein radicals was supported by the finding of a suppurative pylephlebitis post-mortem and by the abscesses—especially the smaller ones—communicating directly with a branch of the portal vein. Infection of the liver by way of the arterial current was improbable. Although Hewlett[2] states that typhoid bacilli are found in the blood in 83 per cent. of the cases of typhoid fever, and Courmont[26] believes that typhoid septicæmia is the rule, the absence of changes in the arteries and the absence of suppurating foci in other parts of the body speak strongly against arterial infection in this case.

Suppuration in the liver following typhoid fever is a rare condition. Holscher reports that 12 cases of liver abscesses occurred in the 2000 fatal cases of typhoid fever at Munich. Romberg reports 1 case of liver abscess from 88 fatal cases of typhoid. Scholtz reports 3686 cases of typhoid fever, 362 of these cases died, and in none of them was suppuration in the liver found. Da Costa[3] has collected 22 cases of liver abscess following typhoid fever. Osler[4] makes the following statement concerning the occurrence of abscesses of the liver following typhoid fever: "Solitary abscess is exceedingly rare and occurred in but 2 cases in my series." Julius Dreschfeld[5] says: "Acute yellow atrophy of the liver and abscess of the liver may be cited as very rare complications." I believe that it is impossible to say, with any degree of accuracy, in what proportion of fatal cases of typhoid fever liver abscess is found. During my experience as a medical student, as an interne in Cook County Hospital, and in private practice, I have knowledge of the post-mortem findings of about 200 cases of typhoid fever. The case herewith reported is the only one in which I believe that suppuration in the liver was found.

The relation of the typhoid bacillus to hepatic suppuration has not been determined. It is possible that the suppuration is due to the presence of the typhoid bacillus alone. I am unable to find the record of a case in which the typhoid bacillus alone was found in a liver abscess that followed typhoid fever. Lannois[6] reports a case from which he isolated the typhoid bacillus, but the colon bacillus was also present. It is true that typhoid bacilli are found in pure cultures in the liver in cases of typhoid fever,[7] but in these cases no inflammatory reaction is present. As yet we have no proof that typhoid bacilli alone are capable of producing an abscess of the liver in patients suffering from typhoid fever. Bindo de Vecchi[8] has shown that the liver is insuscep-

tible to infection with certain organisms. The hepatic resistance may explain the inability of the typhoid bacillus to produce liver abscesses in cases of typhoid fever.

The colon bacillus is, in all probability, the organism that is most active in producing the so-called typhoid liver abscesses. In support of this theory are the following facts:

1. Colon bacilli are present in the abscesses of the liver following typhoid fever.

2. Roger[9] has shown that the liver promotes the growth of the colon bacillus, while it inhibits the growth of the typhoid bacillus.

3. Macaigne and Kleck[10] have shown that the virulence of the colon bacillus is increased by disorders of the intestinal tract.

4. Sanarelli[11] found that colon bacilli, isolated from typhoid stools, were more virulent than when isolated from healthy stools. He thought that the increase in virulence is due to the effect of the typhoid toxins, and devised an ingenious experiment which seems to prove this point. If it is true that the virulence of the colon bacillus is increased in a patient suffering from typhoid fever, and that the liver offers little if any resistance to invasion by the colon bacillus, it is not surprising that hepatic suppuration occasionally follows typhoid fever.

The organisms that are responsible for the production of hepatic abscesses following typhoid fever, reach the liver by way of the portal vein, the hepatic artery, or the bile-ducts. Infection through the portal vein seems to be the most common. In these cases it is probable that the organisms reach the portal vein from the intestinal walls or from the mesenteric glands. They are lodged in the portal radicals in the liver and there begin the process of abscess formation. In these cases the liver is usually diffusely enlarged and many abscesses are found. The abscesses have a well-defined wall—or lining membrane—and the smaller ones can be seen to directly communicate with the branches of the portal vein. The liver tissue surrounding the abscess, especially the smaller ones, does not show marked inflammatory reaction. Usually the findings in the liver are independent of changes in other parts of the body, and suppuration in other organs is uncommon in hepatic abscesses following pylephlebitis. The cases reported by Lannois, Osler, Romberg, Gerhard, Trougel, Buckling, Asch, and Bernhard and the case herewith reported are examples of portal vein infection.

Abscesses of the liver—following typhoid—due to infection by way of the hepatic artery are more rare than the variety described in the foregoing. Cases, however, are reported by Louis, Chvostek, Sidlo, and Barth. In these cases the liver may or may not be enlarged. If enlargement does occur it is rarely uniform. The abscesses are usually single or few in number. They are apt to be of large size, with no

well-defined lining membrane and not connected with the portal vein radicals. Abscesses in other regions of the body is the rule and not the exception. There was an abscess in the parotid in Louis' case. Suppurative perichondritis of the larynx was found in Chvostek's case; and in Sidlos' case an abscess was found in the mastoid region. In these cases it is probable that the colon bacillus as well as the typhoid bacillus is floating in the blood stream. I make this statement because such cases are rare and typhoid septicæmia, as Hewlett and Courmont (loc. cit.) have shown, is common.

The third method of infection of the liver, with abscess formation, namely, by way of the bile tracts, is not common. Klebs alone reports a case of this character. Suppurative cholangitis occasionally follows typhoid fever, but I am unable to find reports of cases of well-defined liver abscesses following typhoid fever in which the organisms have been carried to the liver by the bile channels. The pus in these forms of abscess, described in the foregoing, is usually of a white or yellowish-white color. I can find records of hemorrhagic or dark-colored pus occurring only in cases where secondary pyosepticæmic abscesses were present—that is, where abscesses were ruptured either by operation or by invading some cavity of the body. In these cases the abscess cavity has no "pyogenic membrane," the pus usually contains blood and is dark colored, and the liver tissue surrounding it shows marked inflammatory reaction. The abscess found in the posterior part of the right hepatic lobe in the case herewith reported was one of this character.

The symptoms of hepatic abscess following typhoid fever are: 1. The general symptoms of an infection. 2. Local manifestations pointing to involvement of the liver. Occasionally there are no symptoms complained of that would indicate hepatic involvement. Such cases are recorded by Theodore Dunin[12] and by Osler.[13]

The cases of liver abscess following typhoid that I can find records of occurred in adult males from twenty-five to thirty-seven years of age. One case occurred in a boy, aged twelve years, and another in a girl, aged eleven years. In none of the cases was there a history of previous disease involving the liver.

The first indication of involvement of the liver was manifested by pain in the hepatic region, accompanied by chills and fever. These symptoms occurred in all of the cases that I have reported, except the two mentioned in the foregoing, in which no symptoms referable to the liver were present. The pain and chills usually came on about twenty-five days after the onset of the illness. In one case[14] they occurred as early as the thirteenth day; and in two cases—Lannois[15] and the case herewith reported—they did not appear until the forty-second day.

Pain was present in all of the cases but two. It was usually of a

severe, sharp character, but in some cases was described as being dull. It was usually located in the region of the liver; was generally increased by inspiration, and in one case[16] was aggravated by taking food. In no case was the pain intermittent or paroxysmal; and in no case did it cease until the pus was relieved from tension, either by spontaneous rupture,[17] [18] or by operation. Violent, prolonged, and repeated chills were present in most cases. Dunin[12] mentions the absence of chills in his case. In no case did the chills present the regularity that might be expected in malaria.

Jaundice was by no means a constant symptom. Da Costa[3] reports jaundice in 7 of the 22 cases that he has found recorded. It was present in the cases reported by Romberg,[19] Kohts[8] (Case I.), Sidlo,[17] Petrina,[14] Louis,[20] Chvostek,[21] and Burder.[22] In these cases jaundice occurred as early as the thirteenth day,[14] and as late as the thirty-ninth day[17] after the beginning of the illness. Jaundice occurred in cases with abscesses in other portions of the body,[17] [18] and in cases where suppuration was found only in the liver. It does not appear that jaundice is present more often in cases of pylephlebitis than in cases of infection by way of the hepatic artery.

In most cases the liver was enlarged. Usually the enlargement was diffuse, but in some cases the right lobe was affected alone. In Bauder's, Lannois', and Dunin's cases no enlargement of the liver was found clinically or at post-mortem examination. In Gerhard's case,[23] fluctuation was present over the right hepatic lobe. In all cases where the liver was enlarged, marked tenderness was present.

Ascites was present in one case of pylephlebitis,[6] but no record of ascites is found in a similar case reported by Asch and Bernhard.[24]

No constant or characteristic condition was found in the spleen. Mention was made of its being enlarged in 3 cases. Thrombosis was found in the splenic veins in Lannois' case. I have not found record of splenic suppuration occurring in any case.

Suppuration in portions of the body other than the liver occurred in 7 of the cases. These may be divided into two classes: 1. Suppuration in the mesenteric glands. 2. Suppuration in other portions of the body. In the cases described by Romberg, Kohts, Louis, and the one herewith reported, suppuration was found in the mesenteric glands. Cases coming under Class II. may be divided into two groups: 1. Cases complicated by empyema. 2. Those associated with pus foci in distant regions of the body. I make this division because it is possible that a right-sided empyema might occur by direct extension from hepatic suppuration; while abscesses in distant portions of the body would suggest the carrying of the infection by the blood current.

Empyema occurred in the case described by Osler, and in the one herewith reported. Serous pleuritis was present in the cases reported

by Lannois and by Gerhard. In none of these cases did the hepatic suppuration indicate infection by the arterial supply.

Suppuration in distant portions of the body occurred in the cases described by Louis, suppuration in the parotid gland; by Chvostek, suppurative perichondritis; by Sidlo, pus in the mastoid, temple, and right axilla.

Very little can be found relating to urine, blood, and stool examinations in the reports of these cases. The findings in the case herewith described have been given.

Examination of the contents of the abscess cavities revealed pus of a light color in all cases except in those in which secondary pyosepticæmic abscesses were found. In these the pus was of a dark color. In cases where bacteriological examinations were made the colon bacillus was found. Lannois found the typhoid bacillus also in his case. A micrococcus was found by Dunin, and a staphylococcus was found in Romberg's case.

The symptoms in cases of abscess of the liver following typhoid fever extend over a variable period of time. Gerhard's case died on the fifty-fifth day; Romberg's on the thirty-second day, and the one that I described on the one hundred and first day. Most of the cases died from exhaustion. Dunin's case terminated suddenly. Osler's succumbed to peritonitis. Occasionally cases recover. Sidlo's case passed pus in the stools on the eighty-fourth day and was well on the one hundred and twenty-eighth day. Koht's case had, on the eightieth day, twenty bowel movements containing pus, and recovered on the one hundred and twentieth day. The cases that recovered were doubtless, from their histories, liver abscesses following pylephlebitis. French states that suppurative pylephlebitis may terminate in recovery. Treves[25] has operated on a case of suppurative pylephlebitis that recovered. I cannot find records of a case of hepatic abscess of arterial origin that got well. The prognosis in cases of hepatic suppuration following typhoid fever is always grave, and death may be expected in all cases associated with foci of suppuration in other portions of the body.

The diagnosis may be easy, difficult, or impossible. In Dunin's case the patient died suddenly without any symptoms indicating hepatic involvement. Pain in the hepatic region, chills, and enlargement and tenderness of the liver would suggest hepatic suppuration. Pylephlebitis might produce the same symptoms as hepatic abscess, and cannot be distinguished from it. Aspiration of the liver should be used as diagnostic aid.

The treatment of hepatic suppuration following typhoid fever is surgical. In all cases where a solitary abscess can be diagnosed, the pus should be evacuated by operation. Surgical interference is advised

against in cases of multiple abscesses of the liver. However, I believe that hepatic drainage would relieve the patient somewhat, and might be of value in some cases.

CASE I.—(Lannois, *Revue de Médecine*, 1895, p. 913). The patient was in bed with typhoid for five or six weeks. After the temperature had been normal for three days, he had chills and fever, and ten days later had pain in the liver and stomach. These symptoms continued. The urine contained albumin. He became emaciated and died without being jaundiced or without the liver becoming enlarged.

Autopsy. The liver weighed 1800 grammes. Twelve abscesses containing yellow pus were found in the hepatic substance. Peritonitis was present. Thrombi were found in the mesenteric and portal veins and in the spleen. Peyer's patches were found in the stages of ulceration, healing, and pigmentation. The appendix was adherent, and one ulcer was found in its lumen. The biliary apparatus was normal. Right serofibrinous pleuritis was present. Typhoid and colon bacilli were found in the hepatic abscesses.

CASE II.—(Osler, *Transactions of the Association of American Physicians*, 1897, vol. xii.). A man, aged thirty-seven years, suffered from septic symptoms. Three months previously he had had typhoid. Death resulted from peritonitis without symptoms of hepatic involvement.

Autopsy. Peritonitis. Appendix perforated. Pus in the mesentery. Empyema on the right side. The liver was large and contained many abscesses. Suppurative pylephlebitis was present. The splenic vein was thrombosed.

CASE III.—(George S. Gerhard, *Medical News*, July, 1886). A man, aged twenty-six years, suffered from typhoid. On the twenty-first day the liver became large and tender and he suffered from diarrhœa. Chills developed and were accompanied by fever; later fluid appeared in the right pleural cavity. The patient declined rapidly. Fluctuation was found over the liver, and he died on the fifty-fifth day of his illness.

Autopsy. One large and many small abscesses were found in the liver. Fluid was present in the right pleural cavity. Peyer's patches were involved. The biliary apparatus seemed normal.

CASE IV.—(Prof. Kohts, *Berliner klinische Wochenschrift*). A boy, aged eleven years, had typhoid. His temperature was normal on the thirtieth day. Two days later he had a chill, which was followed by pain in the liver, repeated chills and fever, jaundice, and hepatic enlargement. Eighty-four days after the onset of the illness he had a sudden pain in the abdomen followed by the passage of pus through the bowels. The patient recovered after being sick one hundred and twenty days.

CASE V.—(Prof. Kohts, *loc. cit.*). A patient, aged twelve years, had the symptoms of typhoid. On the twenty-fifth day he had a chill which was followed by pain in the region of the liver. At the same time hepatic enlargement and tenderness over the entire abdomen became manifest. Death occurred on the thirty-first day of the illness.

Autopsy. The liver was enlarged and contained many abscesses. Thrombi were present in the portal vein. Suppuration was present in the mesentery. No abnormal changes were found in the biliary

apparatus; 100 grammes of fluid were found in the pericardial cavity. Peyer's patches were pigmented.

Case VI.—(Romberg, *Berliner klinische Wochenschrift*, March 3, 1890). A man, aged thirty-seven years, suffered from an ordinary attack of typhoid. On or about the eighteenth day of his illness he had a chill, which was followed by sweating, fever, pain in the liver, jaundice, enlargement of the liver, and tenderness over the hepatic and abdominal regions. His spleen was palpable. These symptoms progressed rapidly, and he died on the thirty-fourth day of his illness.

Autopsy. The liver was enlarged and contained many abscesses. Thrombi were found in the portal vein and in the hepatic artery. Peyer's patches were involved. Pus was found in the mesentery of the cæcum. Pneumonia was present, involving the lower lobe of the right lung. A staphylococcus was found in the hepatic abscesses.

Case VII.—(Louis, *Fievre Typhoide*, 1841, vol. i., obs. xvii.). The patient suffered from an ordinary attack of typhoid fever. During the decline of the fever he developed chills, fever, enlargement and tenderness of the liver, and jaundice. The patient died shortly after the appearance of these symptoms.

Autopsy. The liver was enlarged and contained one large abscess and six smaller ones. Peyer's patches were involved. Pus was found in the glands of the mesentery and in the parotid gland.

Case VIII.—(Chvostek, *Med. Chirurg. Rundschau*, June, 1868, p. 1888). This was an ordinary case of typhoid fever that developed septic symptoms, with pain and tenderness in the liver, accompanied by cough and expectoration. Jaundice was present. The patient died from exhaustion.

Autopsy. The liver was found enlarged and contained two large abscesses. The intestines showed evidences of typhoid infection. An abscess was found in the lung. Pericarditis was present.

Case IX.—(Burger, *Lancet*, October 17, 1874). This case differed clinically from the preceding one, in that no hepatic enlargement was present. The patient was jaundiced.

Autopsy. The liver was not enlarged, but many small abscesses were found in the right and left hepatic lobes. No other foci of suppuration were found. The portal vein was thrombosed. Peyer's patches showed evidences of recent involvement.

Case X.—(Sidlo, *Der Militar Aerzt*, Wien, 1875, No. 23, p. 20). This case of typhoid ran an ordinary course until the twenty-third day. Then he had chills, fever, and sweats, with pain and tenderness in the hepatic region, and with enlargement of the liver. He became jaundiced on the thirty-ninth day. Later, abscesses developed in the mastoid, temple, and right axilla. On the eighty-fourth day he developed a diarrhœa, and pus was passed through the bowels. The patient was well on the one hundred and twenty-eighth day.

Case XI.—(Petrini, *Prag. med. Wochen.*, 1888, Nos. 41 and 43). This case of typhoid developed chills and fever, with pain and tenderness in the liver; jaundice and hepatic enlargement on the thirteenth day of his illness. He died from exhaustion.

Autopsy. The liver was large and contained many small abscesses. Thrombi were present in the portal vein. The intestines showed typhoid lesions. No foci of suppuration were found in the body outside of the liver.

Case XII.—(Theodore Dunin, *Deutsche Arch. für klin. Med.*, 1886, Band xxxix., p. 379). A patient, aged thirty-five years, complained of typhoid symptoms and also of a thenar inflammation. The suppuration in the hand opened spontaneously on the fourteenth day of his illness. The typhoid symptoms continued. The patient had no chills; neither did he complain of symptoms that would suggest involvement of the liver. No jaundice or hepatic enlargement were present. On the eighteenth day he got out of bed (was not delirious) to go to the lavatory, and died suddenly.

Autopsy. The liver was not enlarged. It contained many small abscesses. Suppurative pylephlebitis was present. The spleen was markedly enlarged, but no abscesses were found in it. Peyer's patches and the solitary follicles were infiltrated and necrotic. Œdema was present in the lower part of the right lung. The brain was anæmic. A micrococcus and an unidentified bacillus were found in the pus in the liver. No streptococci were present.

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A PRELIMINARY COMMUNICATION CONCERNING THE NATURE AND TREATMENT OF RECURRENT VOMITING IN CHILDREN.

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The nature of the disorder that various authors have called recurrent, periodical, or cyclic vomiting has never been demonstrated, and the treatment has been correspondingly ineffectual. The commonest

theories as to its causation are that it is a neurosis, or that it is due to the so-called gouty or uric acid diathesis. The latter theory apparently has no better basis than the fact that the subjects of the disorder are members of families in which nutritional disturbances are common; while the term neurosis offers no substantial aid in coming to an understanding of the condition.

The observations that I shall report in this article are sufficient to show that in the individual cases to be mentioned there was, at the time of the attacks, but not in the intervals, a severe acid intoxication of the type seen in diabetes mellitus, and occasionally in other conditions. Treatment directed toward this acid intoxication has, in all but one of these cases, been strikingly successful; in the remaining case the result is still in doubt. These facts indicate that a cryptogenic acid intoxication is probably, in many cases, an important, perhaps the most important, element in producing the exhausting and occasionally fatal vomiting. If this proves to be true, proper treatment should often be successful in controlling or preventing the attacks.

The present conception of the importance of intoxication with acids that are produced in the organism has been arrived at chiefly through studies of the intoxication that occurs in diabetes mellitus, and that often leads to fatal coma. It has, however, been definitely shown that this form of intoxication is not confined to diabetes mellitus, but is sometimes seen in other conditions, such as carcinoma, grave anæmia, infectious diseases, and gastro-intestinal disturbances. When recognizable organic disease that is capable of causing acid intoxication is absent, the intoxication is called simply cryptogenic, or acid intoxication *sui generis*. I have recently discussed this condition,[1] and shall now refer to but a few important facts concerning it.

The symptoms that result from acid intoxication may be extremely varied. The most striking symptom that may appear is coma, with the peculiar type of respiration characteristic of this condition; but the intoxication may manifest itself in numerous other symptoms. In the type almost always seen (that in which beta-oybutyric acid is the chief acid present) the characteristic evidences of its existence are the odor of acetone to the breath, and particularly the presence of acetone, diacetic acid, and oxybutyric acid in the urine. The amounts of these substances found, especially of the latter, vary directly with the severity of the intoxication.

It was once thought that acetone produces the symptoms through its specific toxic effects. As is well known, this view has, however, been abandoned long since. It is now believed, on the basis of clinical observation and of animal experimentation, that no specific toxic agent

[1] Phila. Med. Journ., June, 1902.

is at work; but that the symptoms are due merely to the presence of an excessive amount of acids, and are produced by the reduction of the alkalinity of the tissues and of the body fluids, and the loss of alkalies in the excretions, the acids carrying the alkalies off in combination with them. The rational treatment of the condition is, therefore, to administer alkalies in extremely large doses, in order to neutralize artificially the excess of acids present.

Acetonuria has several times been noted in cases of recurrent vomiting. This seemed, however, from the reports to be of little consequence, as acetone and other evidences of acid intoxication frequently appear in the urine, as the result of inanition of any kind, and prolonged vomiting and abstinence from food are sufficient to cause acetonuria or diaceturia. Under such circumstances, the acid intoxication would be purely secondary and would have no importance as a primary factor in the production of the attack.

My interest in acid intoxication as a possible factor in exciting the attacks of recurrent vomiting was aroused by a case seen in January, 1901, the child of a relative from the West. In this case, the attacks had occurred frequently, in spite of rigid dieting and great care of the general health. They showed no definite relation to preliminary digestive disturbances, but were rather closely connected with excitement and overexertion. They had been increasing in frequency, but at the time I saw the child were somewhat less severe than they had been.

In the attack that I observed, the child exhibited, when seen a few hours after the onset of the vomiting, a very marked odor of acetone. This indicated that some degree of acid intoxication was present at the beginning of this attack, and that it might have something to do with producing the symptoms. I was unable to secure urine for examination, but ordered 20 grains of bicarbonate of soda to be given every two hours. The child retained this perfectly; and after four or five doses the vomiting and nausea stopped, and the patient rapidly recovered from the attack.

I then ordered large doses of bicarbonate of soda to be administered at once, if prodromal symptoms should appear at any time; and asked for a specimen of urine at the beginning of an attack if an attack occurred while the child was in this region. No attack has occurred at any time, however. Any suggestive symptoms have at once been treated with alkali, and the child has entirely escaped anything resembling the old attacks.

This case was mentioned in discussion at the meeting of the American Pediatric Society in June, 1902; and my further knowledge of the condition of the urine in these attacks and of the effect of large doses of alkalies is due chiefly to the kindness of Dr. Edward L. Pierson, of Salem, Massachusetts, who communicated with me soon there-

after concerning a case of recurrent vomiting in which he had been closely interested.

In this case, severe attacks, lasting for about a week and causing pronounced exhaustion, had occurred throughout a period of about eighteen months, and had been increasing in frequency. The child's health in the intervals was also growing decidedly unsatisfactory. I suggested examination of the urine for acetone and diacetic acid, and, if these should be found, the use of large amounts of alkali. The urine was first examined on the day of the onset of a typical attack, and both acetone and diacetic acid were found present. Alkalies were administered, and the attack ceased within thirty-six hours. The duration of this attack was about two days and a half, while the customary duration had been six or seven days.

Since that time this child's urine has been almost constantly watched for acetone and diacetic acid; and they have been found to appear together with the prodromal symptoms that had regularly preceded the previous attacks. In each instance except one the immediate use of large amounts of bicarbonate of soda (125 grains in divided doses) has prevented the apparently imminent attack; and in the instance in which this failed, Dr. Pierson believes that the alkali was not given sufficiently early. In a period of about nine months, then, this boy has had only one marked attack besides the one apparently abortive attack at the beginning of the treatment, and his general health has markedly improved.

Dr. Pierson also writes me that he has looked for acetone and diacetic acid in three other cases that he has had under observation, and that he has found these substances present in each case at the beginning of the attack. In all these cases alkalies were administered in the doses mentioned, and in all instances the treatment has been successful in aborting the attacks when used very early.

Dr. Pierson also states that in a further case, not his own, in which he had no opportunity to examine the urine, he suggested this treatment; and that it was used with success. He will himself report these cases in detail; and I shall mention only that he has regularly observed that preceding the attacks there are likely to be either excessive variations in or elevations of the temperature, which are not present when the child is entirely well. He consequently has the temperature taken twice daily, even when the child seems entirely well. If any prodromal symptoms appear, and particularly if the temperature begins to show distinct elevations, he has alkalies administered at once in large doses. He believes that the alkalies do not wholly abort the attack unless they are given before the vomiting has appeared, but considers that they may be depended upon in the cases that he has observed, if given sufficiently early.

I have not been fortunate enough to observe any typical cases since seeing the first one mentioned; nor have a number of pediatrists in Philadelphia who have kindly been watching for cases for me to examine. Recently, however, I have had opportunity to examine the urine of a typical case, subject to very frequent attacks, under the care of Dr. W. T. Sharpless, of West Chester, Pennsylvania. The urine was obtained during the first few hours of an attack. It contained acetone and diacetic acid in large amounts, the acetone being tested for in the distillate, and the diacetic acid test being controlled by boiling and also by extracting with ether. A test for oxybutyric acid by Külz's crotonic acid method yielded very large numbers of crystals in the distillate. The melting point of these crystals, after they had been washed with water and extracted with ether, was determined, and was found in two determinations to be between 71° and 72° C. Oxybutyric acid was evidently present, therefore, in large amounts.

Dr. Sharpless tells me that Mr. John D. Carter, of Haverford College, had twice tested the child's urine for acetone and diacetic acid at the time of an attack; and that he had found these substances present on both occasions. He also found them once in an interval; whether this was near the time of an attack or not was not noted. I had myself once before tested the urine during an interval, and had found it negative.

Dr. Sharpless instituted treatment in this case immediately after my last examination, a drachm of bicarbonate of soda being given three times a day. The attacks of vomiting had subsided when the alkali treatment was instituted, but the child had not become entirely well. After these large doses had been given for about a week the child vomited several times, and this was at first thought to be a mild attack of the usual kind. The vomiting occurred repeatedly at short intervals, however, and Dr. Sharpless concluded that the very large doses of soda were causing local irritation and reduced the dose, giving only enough alkali to keep the urine neutral. Since then, about a month, the child has had no vomiting and is improving in general health. It is, however, too early to decide as to the effect of the treatment.

The facts that I have mentioned concerning the condition of the urine and the effect of treatment demonstrate the presence of a marked acid intoxication in five cases; and probably, also, in the sixth case, mentioned by Dr. Pierson, but not seen by him. The effect of treatment in all the cases, excluding, as yet, that of Dr. Sharpless, makes it seem practically clear that acid intoxication was the chief factor in producing the violent vomiting; and the results of the treatment in five of the six cases have been altogether satisfactory, both to the medical attendants and to the parents, while previously entirely discouraging. I believe that it is probable that similar conditions will be found in at

least a considerable proportion of other cases; and, since other treatment has been extremely unsatisfactory, it is well worth while to try the effect of very large doses of alkali, even if acetone and diacetic acid are not known to be present, but particularly if they are found.

The cause of this acid intoxication can, of course, be only suspected; indeed, we do not definitely know the cause of acid intoxication in any condition. It is highly probable, however, that acidosis is of two varieties: one that is primarily due to a disturbance of metabolism; another that is due primarily to digestive disturbances, but that is perhaps intensified by secondary disturbances of metabolism. It seems very likely that in many cases of recurrent vomiting, and perhaps in all that show acid intoxication, the primary disturbance lies in the digestive tract. I have been unable, as yet, to carry out any studies that might throw light upon this question, as I have not had sufficient control of any case since the activity of acid intoxication in this disorder has come to seem of importance to me. I have, however, studies of this kind in operation, and shall attempt later on to give a broader and more detailed discussion of this question. For the present I may repeat what I have previously said (loc. cit.): that the evidences of acid intoxication have been found in a number of kinds of primary disease and under the guise of a variety of symptoms; that it is a simple matter to look for it; and if found in severe degree it should be treated. Heretofore, in conditions other than diabetes mellitus, interest seems to have been confined to demonstrating its occurrence. In the case of coma that I reported the man recovered from a condition that was desperately grave after enormous doses of alkali had been given intravenously; largely, I believe, as the result of the use of the alkali. In another case, under the care of Dr. S. M. Hamill—a child subject to recurrent attacks of gastro-intestinal disturbance associated with the passage of intestinal sand and not of the type of recurrent vomiting—I recently found the urine during an attack to contain large amounts of acetone, diacetic acid, and oxybutyric acid (crotonic acid test), and the administration of large doses of alkali caused a surprisingly rapid disappearance of the symptoms, while they had been extremely rebellious to other treatment.

Some observations that are in the main practically identical with those presented in this article, but which are not considered by their author in the same light, have been brought to my attention by Dr. J. P. Crozer Griffith. Marfan[1] describes a disorder that is probably identical with the recurrent vomiting of American authors. He states that he has regularly found acetone in the urine in the *beginning* of these attacks. He, however, attributes the condition to "acetonæmia."

[1] Arch. de Méd. des Enfants, 1901.

He doubts the correctness of the modern view that acetonuria indicates acid intoxication, considering that the meaning of acetonuria is wholly in doubt. He prefers to call the condition described by him "vomiting with acetonæmia."

These observations are, I believe, confirmatory of my view that acid intoxication exists in this disorder, for Marfan's interpretation of the observations is certainly incorrect. It has been well established that acetone is not the cause of the toxic symptoms in the form of intoxication in which it appears; that acid intoxication is present in cases associated with acetonuria; that it causes severe toxic symptoms; and that many of the toxic symptoms may be overcome or controlled for a long time, even in diabetes mellitus, if treatment with alkalies is begun early enough. It is even extremely questionable whether "acetonæmia" ever occurs, for it is at present doubtful whether acetone is ever excreted as such or appears only after the excretions leave the body as the result of oxidation of diacetic acid. Marfan rather unwillingly admits that acid intoxication may have something to do with the condition, and he consequently administers milk of magnesia in doses of "two centigrammes." This is probably a printer's error for two decigrammes; but the latter amount—about three grains—would be utterly ineffectual, even though it were absorbed, in case acid intoxication were present. Indeed, it would take but a very little gastric juice to neutralize such amounts. If this treatment is to be used at all some readily diffusible alkali, such as sodium bicarbonate or citrate, should be chosen, and extremely large doses should be given as soon as the first suggestion of an attack is observed; 100 grains, given as rapidly as possible, is probably a low limit. It is best to keep up the rapid administration of large doses until the urine is decidedly alkaline and then keep the urine alkaline until the symptoms have disappeared; and frequent moderately large doses would certainly be better than the occasional use of extremely large doses. During the interval one should give enough alkali to keep the urine about neutral. The doses of alkali commonly employed for other conditions will not demonstrate whether the treatment is effectual or not.

I wish it to be clearly understood that I am prepared to find that recurrent vomiting is not always due to acid intoxication: It is highly probable that the attacks that we call recurrent vomiting are not always dependent upon the same primary disorder. It will, however, be an easy matter to determine in how many cases this form of intoxication is present, and how frequently flooding the organs with alkalies will prove to be an effectual treatment.

UNILATERAL RENAL HÆMATURIA.[1]

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Blood may appear in the urine from various causes, some local, others general in operation. Among the former are congestion, inflammation, embolism, thrombosis, traumatism, retention, parasites, calculi or sand, tuberculosis, and new-growths, involving any portion of the urinary tract. The general causes for hæmaturia include certain infectious diseases, such as variola, measles, scarlet fever, typhoid fever, yellow fever, malarial fever, plague, and pneumonia; certain blood diseases, such as hæmophilia, scurvy, purpura, and leukæmia; certain forms of intoxication, such as that due to cantharides, to turpentine, to mercury, and to quinine, as well as intense jaundice. Hæmaturia has been observed also in cases of hysteria, in association with pregnancy and lactation, and in the sequence of violent physical exertion, and of sexual excess. Occasionally the cause of the condition is not obvious, and under such circumstances it has been variously described as essential or idiopathic hæmaturia, hæmaturia without lesion, hæmaturic nephralgia, renal hæmophilia, local hæmophilia, hæmophilic hæmaturia, angioneurotic hæmaturia. Cases of this sort, however, have become progressively less frequent in proportion as careful anatomical study is undertaken. In some instances the symptoms have pointed to involvement of one kidney; in a number the blood has been seen with the aid of cystoscopy, or of ureteral catheterization, or of direct inspection after cystotomy escaping from the corresponding ureter; and in many relief has followed operation on the kidney—sometimes simple manipulation, at other times nephropexy, at still other times nephrotomy, and at yet other times nephrectomy. Not rarely the kidney has appeared normal, even on section, but often more careful scrutiny has disclosed some abnormal condition, such as displacement or mobility of the kidney, obstruction of the ureter, the existence of pregnancy, the presence of calculi or sand, of tuberculosis, of neoplasm, or of the lesions of chronic nephritis.

I wish to report a case presenting symptoms of renal calculus, with hæmaturia, in which, after the kidney was exposed, found apparently healthy and left undisturbed, the symptoms disappeared permanently.

A girl, twenty years old, employed as a sewing-machine operator in a shirt factory, presented herself on account of constant pain in the

[1] Read before the Medical Society of the State of Pennsylvania, September, 1902.

right side of the abdomen, radiating to the right lower extremity and sometimes over the entire abdomen, with acute paroxysmal exacerbations persisting for from ten days to two weeks, and then gradually subsiding. During the exacerbations the urine assumed a red color supposed to be due to the presence of blood. These symptoms had been present for twelve years, since the age of eight. Urination was not increased in frequency, and was attended with mitigation of the pain. The appetite was impaired, but the pain was uninfluenced by the ingestion of food. There was no vomiting and the bowels acted regularly. There was freedom from cough, expectoration, and œdema. Sleep was not disturbed. The patient complained of frontal headache and of pain in the chest and in the left lower extremity. Menstruation began at thirteen, and had always been regular and unattended with pain, but was profuse. There had been slight loss in weight, but no undue perspiration. The patient, however, appeared well-nourished and her color was good. There was nothing noteworthy in the family history or in the past personal history. The urine presented a red color, an acid reaction and a specific gravity of 1022. It contained a considerable amount of albumin, but no sugar. On microscopic examination a large number of red blood corpuscles were found, together with a moderate number of epithelial cells, a few leucocytes, many crystals of calcium oxalate and granular tube casts. The condition was looked upon as one of renal calculus, and the patient was admitted to the Polyclinic Hospital. The urine at this time was at first bloody, but subsequently it became clear, although microscopic examination continued to disclose the presence of red blood cells.

Dr. L. W. Steinbach, who saw the case in consultation with me, concurred in the diagnosis, and accordingly the right kidney was exposed, but nothing abnormal was found in this organ or the surrounding tissues. The organ was replaced, and surgical recovery was uneventful. The urine was bloody for a short time after the operation, and on several occasions the patient passed a number of somewhat ovoid concretions, the largest of which was 5 mm. in the long and 3 mm. in the short diameter. These were dark red in color and smooth on the surface, some presenting a dull and others a lustrous appearance. They floated on the surface of water, in which, however, they failed to dissolve. They were insoluble also in acids and in alcohol. On microscopic and chemical examination they were found to contain, in addition to red blood corpuscles, crystals of calcium oxalate, phosphates, cystin, and other substances not yielding the reactions for uric acid. Examination of the blood after the operation showed the hæmoglobin percentage to be 78, the number of red blood corpuscles 4,316,000, and the number of leucocytes 9000 in the cubic millimetre. Pain in the right loin persisted for a considerable time, and micturition was attended with burning, but the urine shortly became free from abnormal content, and the patient stated that she felt better than she had at any time in the previous ten years. There had been no recurrence of the hæmaturia a year after the operation, and more than a year has elapsed since the last report.

I have seen the patient within a few days, and while there has been no return of the hæmaturia, micturition is reported to be attended with a sense of burning, and a precipitate is said to be deposited from the urine. Some of the latter brought to me presents a whitish pulveru-

lent and granular appearance, is hard and gritty to the touch, and does not dissolve readily in water. On microscopic examination it is found to consist of granular matter without crystalline form.

Briefly summarized, we have here a case in which the recurrent hæmaturia, with paroxysmal exacerbations of pain in the right loin, extending over a long period of time, without marked wasting or cachexia or evidence of other disease, seemed to point clearly to the presence of a calculus in the right kidney or its pelvis. Operation, however, with exposure and manipulation, though without incision, of the suspected organ failed to disclose the presence of a foreign body or of any other abnormality. The presence of albumin, tube casts, and crystals of oxalates in the urine prior to operation suggests the existence of irritation or inflammation of the kidney, while the small concretions that were discharged after the operation, and consisting principally of blood clot, although they contained other matters, would seem to have been a result rather than the cause of the bleeding. Although the evidence is not conclusive, it is safe to assume that the blood came from the right kidney alone. This view is sustained by the cessation of the hæmaturia after exposure and manipulation of this organ, although no underlying cause was discovered, and, therefore, nothing further was undertaken with the definite object of effecting its removal. It may be conceived that as a result of the necessary operative manipulations fine sand-like particles or minute calculi were dislodged, and thus a source of irritation removed, or that certain changes were thereby brought about in the circulatory conditions of the kidney, but neither of these explanations is entirely satisfactory. The long duration and the subsequent recovery militate against malignant disease and tuberculosis, and there was no indication of hæmophilia. The case must, therefore, be looked upon as an example of hemorrhage from one kidney of obscure origin, with cessation of the hæmaturia in the sequence of surgical intervention involving only exposure and manipulation of the suspected organ.

I have succeeded in collecting from the literature a number of cases of similar or related character.

The *British Medical Journal* for May 18, 1872, pp. 534 and 565, contains references to an operation undertaken by Mr. Durham upon a woman, aged forty-three years, with the expectation of finding a calculus in or about the pelvis of the right kidney. No calculus being found, and the kidney appearing healthy, the organ was returned and the wound closed. Pain, hæmaturia, and other symptoms, however, persisting for more than two years after the operation, nephrectomy was performed, but the patient died a short time afterward.

C. Lauenstein[1] relates the case of a sailor, forty-seven years old,

[1] Deutsche medicinische Wochenschrift, June 30, 1887, p. 56.

who for twelve years suffered from constant pain in the right loin, with paroxysmal exacerbations and profuse hæmaturia. The urine contained red and white blood corpuscles and crystals of lime salts. The right kidney was exposed, its pelvis opened, puncture made in three places, but nothing abnormal was detected. The urine became clear in the course of a few days and remained so.

William Anderson[1] reports the case of a woman, twenty-four years old, who for four years had had recurrent attacks of hæmaturia, with pain in the right loin and groin. Renal calculus being suspected the right kidney was exposed, palpated, and punctured, but no abnormality was found. The patient was better for a time, but the symptoms returned in the course of a month, although permanent improvement subsequently ensued. The case was considered an example of some complicated form of neurosis.

Under the designation of hæmaturic nephralgia, A. Sabatier[2] has reported the case of a woman, thirty years old, who for seven or eight years had had attacks of oppression, with œdema of the lower extremities, especially on the right side, and a painful swelling in the right flank. The urine was at first chocolate colored and contained blood, but no tubercle bacilli. Later there developed headache, vomiting, nausea, and pain in the right flank. On palpation over the right kidney pain was induced, but no tumor could be distinguished. The urine was now scanty and bloody. An attack of uræmia occurred and was relieved by bleeding. The hæmaturia became gradually more marked, clots at times appearing in the urine, but the general health remained good. The pain in the right loin increased to such a degree as to prevent recumbency on that side. It was induced by walking and by inclination of the body to the right side, and it radiated in paroxysms to the ureter, the bladder and the lower extremities. The symptoms were thought to be due to calculous pyelitis, the stone occluding the ureter from time to time. Accordingly, operation was decided upon and the kidney was exposed through a lumbar incision and divided down to its pelvis, but no stone or neoplasm was discovered, although a sound was introduced into the ureter. On account of the profuse hemorrhage, and with a view of causing obliteration of the ureter in case that structure was the seat of the lesion, the kidney was removed. The patient made a speedy recovery, and the hemorrhage had not recurred two years after operation. Examination of the removed organ disclosed no abnormality.

M. Schede[3] has reported the case of a robust man, fifty years old, without hereditary predisposition, in whom hæmaturia appeared in the sequence of the ingestion of a cold drink. There was at first a sense of coldness in the left lumbar region, and later transient pain of moderate severity in this situation and in the bladder. The bleeding recurred when the patient assumed the erect posture and ceased in the recumbent posture. It grew progressively more marked until it could no longer be prevented by even the most absolute rest. The patient had been kept in bed for four weeks, but the urine had been continuously bloody for one week. The general condition had not suffered greatly, although there was slight wasting. There was no fever.

[1] Lancet, April 20, 1889.

[2] Revue de Chirurgie, 1889, ix. p. 62.

[3] Jahrbuch der Hamburger Staatskrankenanstalten, I. Jahrgang, 1889, p. 235.

Neither kidney could be made out on palpation, and nothing abnormal was found on examination of the bladder with the aid of the sound and the endoscope. The urine contained red and white blood corpuscles and ciliated epithelial cells. Styptics were administered, but without relief. Three possibilities were considered: 1. A calculus in the pelvis of the kidney causing erosion of the bloodvessel. 2. Primary miliary tuberculosis. 3. Beginning malignant disease.

On account of the persistence of the hemorrhage operation was decided upon, and in order to determine if possible which kidney was the seat of the disease suprapubic cystotomy was performed, and each ureter catheterized. By this means it was learned that the blood came from the left kidney. Accordingly, this organ was exposed, but it was found normal in form and size, and neither stone nor tumor could be detected, even after incision of the renal pelvis. It was decided that in order to prevent further hemorrhage it would be best to remove the kidney, and this was done. The wound united without complication and the hæmaturia was not repeated. The removed kidney was found to be friable and anæmic, and the seat of small petechiæ. Microscopic examination disclosed the presence of isolated, almost disintegrated tube casts, covered with red blood corpuscles.

Schede suggests the name of local hæmophilia for the condition, but it seems not impossible that the kidney was the seat of an inflammatory process.

Under the title of renal hæmophilia, H. Senator[1] describes a case of hæmaturia of two and one-quarter years' standing in a girl, nineteen years old. At first the urine was discolored in connection with menstruation, and at this time it contained only hæmoglobin, but no red blood corpuscles. Later red blood corpuscles made their appearance, and the hæmaturia occurred independently of menstruation and without pain. There was slight increase in the frequency of micturition, but no bearing down or tenesmus. Anæmia and slight cough suggested the possibility of tuberculosis, but there was no fever and little wasting.

The case was looked upon as one of hæmophilia, as the patient had four brothers and sisters who exhibited a marked tendency to epistaxis, while the father had from youth suffered from the same condition and also from hæmoptysis without evidence of disease of the lungs, and eleven of his brothers and sisters, as well as other and more distant relatives also suffered from epistaxis, and among the women profuse menstruation was common.

Physical examination failed to disclose any evidence of visceral disease, while with the aid of the cystoscope blood could be seen entering the bladder from the right ureter. As the patient was growing progressively worse, and in order to avert a fatal issue, the right kidney was removed. The urine was bloody for a day or two after the operation, but thereafter it became and remained clear. The wound healed without complication, and the patient was dismissed as well after four weeks. On microscopic examination extravasations of blood were

[1] Verhandlungen der Berliner medicinischen Gesellschaft aus dem Gesellschaftsjahre, 1890; Separat-abdruck aus der Berliner klinischen Wochenschrift, 1891, B. xxi. p. 293.

found in the removed organ, and lesions of slight circumscribed interstitial nephritis—a condition thought to be characteristic of hæmophilia. Senator considers hæmophilia a congenital hereditary tendency to hemorrhage, which may be local as well as general.

This case must be considered as one of nephritis rather than one of hæmophilia in the strict sense of the word, as the patient herself exhibited no undue tendency to hemorrhage apart from the hæmaturia, and the histological examination revealed the lesions of the former condition.

Robert Abbe[1] exhibited to the Section on General Surgery of the New York Academy of Medicine a patient who, five years previously, had begun to suffer from renal colic and hæmaturia, which continued for two years. The hemorrhage had recurred within six weeks, and cystoscopic examination showed that the blood came from the right ureter. The right kidney was exposed and found normal. It was stripped of its capsule and fifteen punctures made at different places on the convexity of the organ. At one point only was any sense of abnormality appreciated. In this situation the kidney was incised and a finger introduced into the pelvis of the organ. No stone was found, but the finger came in contact with a gritty point, which it was thought might have corresponded to the papilla of one of the pyramids. The wound was closed without further intervention and the patient was thereafter free from pain and hæmaturia.

F. Legueu[2] reports the case of a man, twenty-six years old, with a neuropathic history, who suffered from recurrent attacks of pain in the left iliac region, generally attended with hæmaturia, and superinduced by exercise and coitus. On examination the left kidney was found to be tender and slightly increased in size. The organ was exposed and found slightly depressed and mobile. It was freed from its capsule and grasped between the fingers, but no abnormality was detected. Temporary relief followed, but death took place in the course of two months. The condition was looked upon as one of idiopathic renal neuralgia in a neuropathic subject.

Albert L. Stavely[3] reports two cases of hæmaturia in which the bleeding ceased in the sequence of an incision of the kidney from which ureteral catheterization showed the blood to be derived. One of the patients was a woman, thirty-nine years old, with a family history of tuberculosis and symptoms of the same disease, who for five years had had intermittent hæmaturia of increasing severity. The urine contained blood, but no tubercle bacilli could be found. Blood was obtained from the left ureter with the aid of a catheter. The bladder had to be incised to gain access to the right ureter. The former appeared healthy, while the urine from the latter contained a trace of blood. The left kidney was exposed and presented an area of doubtful fluctuation along its convex border, but when an incision was made down to the pelvis of the organ careful inspection failed to disclose

[1] Medical Record, May 16, 1891, p. 573.
[2] Annales des Maladies des Organes Genito-Urinaires, August, September, November, 1891.
[3] Bulletin of the Johns Hopkins Hospital, March, 1893, p. 25.

any disease. The hæmaturia ceased after a slight temporary recurrence.

The second case occurred in a woman, in whom the hæmaturia had set in suddenly and had persisted intermittently for a year, growing progressively worse. The urine contained a large amount of albumin, numerous red blood corpuscles, a few leucocytes, a few large epithelial cells, but no casts. On catheterization blood was obtained from the left ureter, while the urine from the right ureter was clear. The left kidney was exposed and incised, but it presented no macroscopic evidence of disease. Histological examination of a bit of removed tissue, however, disclosed lesions of chronic nephritis. The urine contained albumin and blood for a time after the operation, but both eventually disappeared.

J. Israel[1] reports the case of a previously healthy woman, forty-two years old, without hereditary predisposition, in whom three weeks following an attack attended with severe pain in the left chest and a chill, hæmaturia occurred and persisted for eleven days. Both kidneys were palpable, displaced downward, and apparently normal, the left being especially movable and tender. The urine contained red blood corpuscles and renal epithelium. On cystoscopic examination blood was seen escaping from the left ureter. On account of a possibility of the presence of a small tumor the kidney was exposed and incised freely, but no abnormality was found. The halves of the kidney were united by suture and the organ was replaced, and primary union took place. The hæmaturia continued freely for three days, but thereafter it began to subside. On the seventh day only traces of blood were present in the urine, on the eleventh day none whatever, and on the thirteenth day none could be detected microscopically. There was no recurrence of the hæmaturia and the patient remained well. Israel was inclined to attribute the favorable result in this case to the influence of the operation.

A. Broca[2] reports the case of a woman, twenty-eight years old, who had suffered from hæmaturia for sixteen months, together with dull pain in the loins, greater on the right. The urine contained blood, casts, crystals, but no tubercle bacilli. Tuberculosis or neoplasm was suspected, and accordingly the right kidney was exposed, its capsule removed and the organ carefully palpated, but no abnormality was found. The first micturition following the operation was bloody, but subsequently the urine was clear for at least three years.

L. Picque and Th. Reblaub[3] have reported the case of a woman, seventy-six years old, who had suffered from hæmaturia for four months. On examination the left loin was found the seat of pain on percussion, and a large body was appreciable on palpation. When viewed with the cystoscope the bladder appeared to contain a neoplasm, but this proved to be a collection of blood clot, and after its removal the hemorrhage ceased. The left kidney was, nevertheless, exposed, and on removal of its fatty capsule exhibited a voluminous cyst at its inferior pole. This was evacuated and its walls excised. No other lesion was found on careful palpation, and on section the kidney appeared

[1] Archiv für klinische Chirurgie, 1894, Bd. xlvii. p. 428.

[2] Annales des Maladies des Organes Genito-Urinaires, December, 1894, p. 881.

[3] Neuvième Congrès de Chirurgie, Paris, 1895, p. 530.

perfectly normal. The organ was returned to the abdominal cavity and perfect recovery ensued.

At a later date Picque[1] reported that hæmaturia returned after an interval of three years. Cystoscopic examination now disclosed the presence of a tumor in the bladder near the mouth of the right ureter. Suprapubic cystotomy was performed and the tumor removed. Recovery ensued.

Picque and Reblaub have reported also the case of a woman, thirty-nine years old, seen in the service of Professor Guyon, who had suffered from hæmaturia for eighteen months and from shooting pains in the right loin for seven months. On examination the right kidney seemed enlarged and mobile and slightly irregular on its surface, as well as tender. With the aid of the cystoscope blood was seen to escape from the right ureter on pressure over the right kidney. The urine contained a large number of red blood corpuscles and epithelial cells from the bladder, but no tubercle bacilli. The presence of a neoplasm being suspected the kidney was exposed, but no abnormality was found and the organ was replaced. The urine became clear on the day after the operation, and remained so thereafter.

Picque and Reblaub were inclined to look upon the hæmaturia as of vasomotor origin and comparable to the hæmoptysis and epistaxis observed in hysterical individuals.

Thomas Oliver[2] has related the case of a sailor presenting profuse hæmaturia, with pain in the left loin. The bladder being found normal on examination, the left kidney was exposed, probed, cut, and examined, but no stone was found. The organ was replaced, but the patient failed to rally. At autopsy no microscopic evidence of disease could be detected, but histological examination disclosed lesions of interstitial nephritis.

In another case cited by Oliver, a man, fifty-four years old, suffered from paroxysmal pain in the right loin, with hæmaturia. When the right kidney was exposed it was found greatly shrivelled, but no calculus could be detected with the aid of a needle. The hæmaturia ceased in the course of a few days, and there was no return during the remaining seven or eight years of the patient's life.

George Elb[3] reports the case of a man, twenty-two years old, who had two attacks of hæmaturia a year apart. On cystoscopic examination the blood was seen to come from the left ureter, while the urine from the right ureter was clear. The left kidney, when removed, presented no lesion, and there was no further return of the hæmaturia. This case is reported—as one of angioneurotic hæmaturia—also by G. Klemperer[4] in the course of a paper on "Hemorrhage from Healthy Kidneys," read before the Berlin Society for Internal Medicine. In the discussion of this communication Nitze[5] stated that he had operated upon seven cases of "essential hæmaturia," dividing the kidney in three and removing it in four. Recovery ensued in all.

F. Guyon[6] reports the case of a man, twenty-six years old, with a

[1] Bulletin et Mémoires de la Société de Chirurgie de Paris, 1898, vol. xxiv. p. 594.
[2] International Clinics, 1895, vol. iii. 5th series, p. 59.
[3] Inaugural Dissertation, Berlin, 1896.
[4] Deutsche medicinische Wochenschrift, February 25, March 4, 1897.
[5] Vereins-beilage der Deutschen medicinischen Wochenschrift, February 18, 1897, p. 54.
[6] Annales des Maladies des Organes Genito-Urinaires, February, 1897, p. 113.

history of malarial fever, who suffered from three attacks of hæmaturia in the course of nineteen months. On examination the right kidney appeared enlarged and irregular, and with the aid of the cystoscope blood could be seen coming from the right ureter. The urine was purulent and contained tubercle bacilli. On rectal examination nodules could be felt at the base of the prostate gland. The right kidney was thought to be tuberculous, and accordingly it was exposed and divided. In spite, however, of most careful search no lesion could be found and the organ was sutured and replaced.

Guyon reports also the case of a woman, thirty-five years old, who suffered from hæmaturia during her second and third pregnancies, with a recurrence while nursing the last child. There was pain in the right loin and the corresponding kidney appeared enlarged and irregular. Lactation was suspended and the hæmaturia ceased at once. The right kidney, being thought to be carcinomatous, was exposed, found normal, and replaced. There was no return of the bleeding. Guyon believed the hæmaturia to be the result of congestion of the kidney.

De Keersmaecker[1] reports the case of a woman, forty-three years old, who had suffered for many years from painful micturition, and for two years from hæmaturia in varying degree. The urine contained blood cells, but no tubercle bacilli or tube casts or renal elements. On cystoscopic examination the bladder was found normal, but the ureteral orifices could not be seen. A catheter was, however, introduced into each ureter and it was found that the blood came from the left kidney. As this organ appeared enlarged, it was exposed, found mobile, and removed. There was no subsequent return of the hæmaturia. The organ was found the seat of chronic nephritis.

Debaisieux[2] has reported the case of a woman, twenty years old, who for six months following an attack of influenza suffered from hæmaturia, with colicky pain in the left half of the abdomen, loin, and iliac fossa. The urine contained blood cells and a corresponding amount of albumin, but no casts or crystals. The presence of a calculus or a neoplasm being suspected, the kidney was exposed, incised, and examined, and two translucent prominences, as large as a pin-head, were detected on the mucous membrane of the renal pelvis. The urine became clear three days following the operation, and was still so two and one-half years later.

In discussing the report of this case, Dandois[3] related the case of a woman, thirty years old, suffering from hæmaturia of sudden onset, with colicky pain in the right loin. Nephrotomy was performed, and the kidney found only the seat of congestion. The bleeding and the pain ceased and did not return. The further course of the case proved that the patient had been pregnant for one week before the occurrence of the hæmaturia.

Gallet[4] referred to a case of mobile kidney with hæmaturia in which relief was afforded by nephropexy.

M. L. Harris[5] reports the case of a farmer, fifty years old, who had suffered from hæmaturia for three years. Cystoscopic examination showed that the blood came from the left ureter. The urine contained blood corpuscles and a small amount of albumin, but no tube casts.

[1] Annales de la Société Belge de Chirurgie, 1897, p. 159.
[2] Ibid., p. 205. [3] Ibid., p. 215. [4] Ibid., p. 219.
[5] Philadelphia Medical Journal, March 19, 1898, p. 508.

The condition was thought to depend upon an angioma of the renal pelvis or of the kidney itself, or to be one of angioneurotic hæmaturia. Medicinal treatment failing to yield relief, the kidney was exposed, but found normal in every respect. Nevertheless, the organ was divided, but no abnormality was found. The kidney was united and replaced, and the urine gradually became clear and remained so.

Genouville[1] reports the case of a man, fifty-one years old, who for a year suffered from attacks of pain in the right loin suggestive of renal colic, and the later of which were followed by hæmaturia. On cystoscopic examination the bladder presented a normal appearance, but blood was seen issuing from the right ureter. A diagnosis of calculus or neoplasm was made, but the corresponding kidney was exposed, found irregular on its surface, elongated, flattened, and empty. Removal of the renal capsule was readily effected, but bleeding followed. The kidney was divided and the parenchyma found of varying thickness, with some fragments of false membrane in the renal pelvis. The condition was looked upon as one of secondary hydronephrosis. At a later date nephrectomy was performed and there was no recurrence of the hæmaturia.

Genouville reports a second case, in a man, thirty-five years old, who suffered from hæmaturia, with pain at first in the left and later in the right loin. The urine at first contained little blood and no albumin, but later albumin and tube casts also were found present. The blood was observed to come from the right ureter, and the corresponding kidney was exposed and found large and hyperæmic. The organ was incised, but only capsular adhesions were found. There was no hæmaturia for a year and a half after the operation, but there was at this time for two or three days a copious admixture of blood with the urine, which again contained albumin and tube casts.

Genouville refers further to two cases of profuse hæmaturia with pain in the loin, the blood coming from the right kidney. When exposed the organ was found only mobile, no lesion being appreciable on incision. Relief followed nephropexy.

Demons[2] has reported the case of a woman, twenty-four years old, who had an attack of colicky pain in the left lumbar region and two years later copious persistent hæmaturia for a period of several weeks. On deep palpation the left kidney was found tender, but not enlarged or displaced. On cystoscopic examination blood was seen escaping from the left ureter. When the kidney was exposed subcapsular ecchymoses and cicatricial depressions came into view. The organ was incised, the cortical tissue found denser than normal, and the renal substance presented a yellowish tint. Nephrectomy was decided upon and performed and there was no return of the hæmaturia. Histological examination disclosed sclerotic changes involving especially the glomeruli and the collecting tubules.

Loumeau[3] has reported the case of a woman, thirty-two years old, subject to rheumatic pains and nasal and hemorrhoidal bleeding, who suffered at first from several slight attacks of hæmaturia under the influence of cold, and thirteen months later from persistent hæmaturia

[1] Annales des Maladies des Organes Genito-Urinaires, 1898, p. 449.
[2] XII. Congrès de Chirurgie, Paris, 1898, p. 408.
[3] Ibid., 1898, p. 413.

for a period of seven months, together with slight pain in the left groin and tenderness on palpation of this region. The urine was found free from tubercle bacilli. On cystoscopic examination blood was seen escaping from the left ureter. When exposed the kidney appeared congested and it was divided, but no lesion was apparent, and the organ was replaced. There had been no return of the hæmaturia at the time of report, four months after operation, and reference is made to the case also at a later date.[1]

Debersaques[2] reports the case of a fisherman, thirty-eight years old, who suffered for twenty years from pain in the left loin, for eight years from intermittent hæmaturia, and for three years from violent and paroxysmal pain in the left loin, inguinal region, and genitalia. Microscopic examination disclosed the presence of blood corpuscles in the urine. On palpation in narcosis the left kidney was found slightly mobile, and pressure caused slight pain. The organ was exposed and incised and found congested. A sound was introduced into the ureter, but no abnormality could be detected. The hæmaturia ceased after the first day following the operation.

Poirier[3] has reported the case of a woman, forty-eight years old, who for three months had suffered from hæmaturia, with rapid emaciation and general lassitude. The urine contained a considerable amount of albumin and a large number of red blood corpuscles. On cystoscopic examination pure blood could be seen escaping from the right ureter into the bladder. The presence of a renal calculus was suspected, and accordingly the kidney was exposed and incised. The organ was normal in size, lobulated, granular, and cystic, but no foreign body was found. Nephrectomy was performed. The urine contained much less albumin after the operation and no red blood corpuscles. On histological examination lesions of chronic nephritis were found. Three months later the patient was seized with symptoms of asthma and pulmonary congestion, and death resulted, it is supposed, in consequence of a lighting up of disease in the remaining kidney.

Pousson[4] has reported the case of a woman, twenty-three old years who for five months had had hæmaturia at progressively shorter intervals and in gradually increasing degree. On palpation the right kidney was found displaced and enlarged, but not painful. On cystoscopic examination the urine from the right ureter could be seen to be bloody. In addition to red and white blood corpuscles, it contained albumin and tube casts, but no tubercle bacilli. The condition was, nevertheless, thought to be dependent upon primary renal tuberculosis or upon epithelioma of the pelvis of the kidney. Accordingly the organ was exposed and divided down to its pelvis. The kidney presented an irregularly hyperæmic and anæmic appearance, and its removal was decided upon and effected. On histological examination there were found lesions of chronic nephritis. The hæmaturia did not recur, although the urine continued to contain a trace of albumin.

Potherat[5] has reported the case of a woman, fifty-two years old, who for eighteen months had been suffering from profuse hæmaturia,

[1] L'Association Française d'Urologie, Paris, 1900, p. 125.
[2] Annales de la Société Belge de Chirurgie, July, 1898.
[3] Bulletin et Mémoires de la Société de Chirurgie de Paris, 1898, xxiv. pp. 462, 593.
[4] Ibid., p. 590.
[5] Ibid., p. 634.

resulting in anæmia and compelling the patient to remain in bed. On examination the right kidney was found enlarged, displaced downward, and nodular. The urine contained albumin in small amount. The presence of a neoplasm being suspected, the kidney was exposed and removed. For four days after the operation the patient suffered from anuria. This was temporarily relieved, but it gradually returned and death resulted from uræmia. On histological examination the removed organ presented lesions of an inflammatory character, and the condition was considered one of chronic interstitial nephritis, the disease, however, being more pronounced on the left side.

T. Rovsing[1] reports four cases of hæmaturia in which the bleeding ceased in the sequence of nephrotomy. The first occurred in a woman, twenty-one years old, who from the age of sixteen had suffered from attacks of pain in the right side of the abdomen that were considered to be due to appendicitis, but with which later hæmaturia became associated. On cystoscopic examination blood was seen escaping from the right ureter. The urine contained blood corpuscles, but no tubercle bacilli or other bacteria. On making an incision in the right lumbar region the kidney was found adherent in its upper third and this presented a bluish-red appearance, as did also a section of the organ when divided from its convex border. No other abnormality was found. On the following day the urine was slightly mixed with blood, but on the third day it was quite clear, and from the eighth day it was entirely free from blood. There had been no recurrence of the hæmaturia in eighteen months. Microscopic examination of a bit of tissue removed from the kidney disclosed venous and capillary stasis, in places with small circumscribed areas of necrosis not cuneiform in shape, fresh thrombi in the straight arteries, extravasations of blood in Bowman's capsules, and hyaline casts in the convoluted tubules. The bleeding and the changes in the upper third of the kidney were thought to be due to compression of the organ between the liver and the ribs as a result of tight lacing, the operation freeing adhesions and releasing the organ.

The second case occurred in a woman, fifty-six years old, who, after hard work and heavy lifting, at the age of forty-four noticed the presence of blood in the urine. The hæmaturia was repeated ten years later and again sixteen days before coming under observation. The patient was pallid, emaciated, and cachectic-looking. In the right loin could be felt a large, hard tumor, which was thought to be the enlarged kidney. On cystoscopic examination blood could be seen escaping from the right ureter. The urine contained blood cells and bacterium coli. Through an incision in the right loin the kidney was found displaced downward and occupying an oblique position, with its upper pole directed toward the vertebral column and its convex border forward and upward. The organ was divided from its convex border and presented a cyanotic appearance. No other lesion was discovered and the two halves were sutured, the kidney replaced, and the wound closed. The urine was clear on the following day, and eleven days later it no longer yielded the chemical reactions for blood. After the lapse of six days more the bacterium coli was present, but at the end of two months the urine was sterile. On microscopic examination of

[1] British Medical Journal, November 19, 1898, p. 1547.

a bit of tissue removed from the kidney, venous and capillary stasis was found, with a number of bacilli in the straight tubes. In this case also the displacement of the kidney was attributed to tight lacing.

The third case occurred in a man, forty-seven years old, who had for three months been suffering from hæmaturia, with a dragging sensation in the left loin. Micturition was unattended with pain. The left epididymis was the seat of a flat, uneven infiltration. On cystoscopic examination blood was seen issuing from the left ureter. No tubercle bacilli or other bacteria and no crystals were found in the urine. A tumor or tuberculosis of the left kidney was suspected, but on exposure of this organ it was found situated high up under the diaphragm, but otherwise apparently normal in every respect, even after division. The right kidney also was found healthy. The urine contained blood for two days, but thereafter it was clear.

In this case it is suggested that there was possibly a small tuberculous focus that was overlooked, or some other lesion that underwent cure as a result of the incision.

The fourth case occurred in a woman, twenty-eight years old, who had suffered for four years from pain in the left loin following physical exertion. After a severe exacerbation, in which the pain radiated toward the bladder and was attended with frequent vesical tenesmus, hæmaturia set in and persisted for six days, although subsequently the urine did not become entirely clear. Renal calculus was suspected, but in the absence of a positive diagnosis operation was not undertaken. The patient grew worse, and the pain more severe, and the left kidney became enlarged and displaced. Cystoscopic examination now showed turbid, bloody urine issuing from the left ureter. The urine contained blood corpuscles, epithelial cells, and bacterium coli. On operation the left kidney was found displaced downward, its pelvis dilated and the ureter bent on itself. On division of the kidney turbid, bloody urine escaped. The renal pelvis was irrigated, the wound sutured, and the organ fixed in place. The urine was clear on the second day after the operation. Examination of a bit of tissue removed from the kidney showed this to be normal except for the presence of groups of bacteria in the straight tubes.

T. Myles[1] reports the case of a woman, twenty-six years old, who, shortly after a successful operation for the relief of hemorrhoids, was seized with recurrent attacks of dull, aching pain in the left side of the abdomen, occasionally attended with vomiting. Hæmaturia set in and was attended with progressive emaciation and anæmia. Both kidneys were movable, especially the left, and pressure over the latter caused suffering. The urine consisted of almost pure blood, and it contained no tubercle bacilli. On cystoscopic examination blood was seen escaping from the left ureter. Rest and styptics failing to control the hemorrhage, the left kidney was exposed and found enlarged, congested, and lobulated. The pelvis of the kidney was incised and a long, flexible, metallic bougie was introduced into the ureter. No obstruction was found, and the calices were examined with the finger and the sound, but nothing abnormal was detected. An exploring needle was plunged into the substance of the kidney in various situations, but no lesion discovered. The kidney was fixed in position and

[1] Medical Press and Circular, August 23, 1899, p. 179.

the wound closed, but the hæmaturia persisted. Accordingly the kidney was removed twenty-three days after the primary operation and the hemorrhage thereafter ceased. On histological examination diffuse myxangiomatous change was found in the submucous tissues of the pelvis of the kidney, while the tissues of the kidney were the seat of but slight changes.

E. Hurry Fenwick[1] states that he has in numerous instances observed painless unilateral renal hæmaturia in young persons, without the discovery on nephrotomy and digital exploration of the pelvis of the kidney of a cause for the hemorrhage. He reports two such cases in which when the kidney was opened and exposed to electric illumination a condition of papillary telangiectasis was found, and removal of which was followed by cessation of the hæmaturia.

The one patient was a woman, eighteen years old, who had suffered from intermittent hæmaturia of five years' standing, without the presence in the urine of tube casts, tubercle bacilli, or cells from the renal pelvis. The possibility of hysteria and of calculus was taken into consideration. On cystoscopic examination blood was seen entering the bladder from the left ureter. The corresponding kidney was accordingly exposed, but nothing abnormal was found until the pelvis of the kidney was opened, when, under electric illumination, a tuft of congeries of vessels was seen surrounding the apex of one renal papilla. This was removed and the hæmaturia ceased and the patient recovered. A slight relapse occurred eighteen months later.

The second patient was a woman, thirty years old, who had suffered from profuse hæmaturia for fourteen days without apparent cause. No renal cells, fragments of new-growth, tubercle bacilli, or tube casts were found in the urine. Cystoscopic examination showed the bladder to be healthy, but blood could be seen entering from the left ureter. Accordingly the kidney was exposed and together with the renal pelvis and the ureter it was found normal, but on opening the pelvis a bright red varicose papilla came into view. This was scooped out, the kidney closed and replaced, and there was no return of the hemorrhage.

Pousson[2] reports two cases illustrating the influence of distention of the kidney in the causation of hæmaturia. One occurred in a laundress, aged twenty-nine years, who suffered from pain in the loin, with hæmaturia. On examination the left kidney was found enlarged and painful. With the aid of the cystoscope blood was seen coming from the left ureter. The condition was thought to be dependent upon obstruction of the ureter by a calculus. The kidney was exposed, found to be enlarged, and uronephrotic. It was opened and much fluid escaped. A valve-like fold of the mucous membrane was found at the mouth of the ureter. This was divided and the wound closed, the kidney being sutured in place. The hæmaturia ceased, but infection of the wound resulted and the kidney was subsequently removed.

The second case occurred in a man, thirty-six years old, who had exhibited vague symptoms of renal colic at the age of twelve and hæmaturia at thirty. On examination the left kidney was found slightly enlarged and painful on pressure. With the aid of the cystoscope blood was observed escaping freely from the left ureter. Primary

[1] British Medical Journal, February 3, 1900, p. 248.

[2] L'Association Française d'Urologie, Paris, 1900, p. 100.

renal tuberculosis being suspected the corresponding kidney was exposed and found enlarged and fluctuating. On incision a round calculus extending into the ureter was disclosed. The renal tissue was stretched and thinned. Nephrectomy was performed.

J. Albarran[1] reports a case of hæmaturia attributed to unrecognized nephritis. The patient was a man, fifty-three years old, with pain in the right loin, radiating in the course of the ureter and attended with the presence of a small amount of albumin and at times red blood corpuscles in the urine. In conjunction with an exacerbation of pain copious hæmaturia occurred, and on cystoscopic examination blood was seen coming from the right ureter. A diagnosis of nephritis was made. On exposure of the kidney the organ was found enlarged, hyperæmic, and adherent, and when divided it appeared healthy except for the presence of a grayish nodule, the size of a millet-seed, at the base of a pyramid. This was enucleated and found to present the lesions of chronic nephritis. There was no return of the bleeding.

Loumeau[2] refers to a case of hæmaturia in a woman, thirty-four years old, in whom the blood came from the left kidney. The condition was thought to be due to primary tuberculosis, and as a last resort nephrectomy was performed. The hemorrhage ceased, but uræmic symptoms developed and death resulted in the course of fifteen days.

O. Pasteau[3] reports the case of a woman, forty-four years old, who complained of pain in the right lumbar region and presented signs of downward displacement of the kidney, later attended with hæmaturia. The kidney was exposed and sutured in its proper position. Mild attacks of pain, nevertheless, occurred, but there was no return of the hæmaturia.

Granville MacGowan[4] reports the case of a man, thirty-five years old, who, after lifting a heavy weight eight years previously, had an attack of profuse hæmaturia, which ceased spontaneously in the course of several days. Within two months the hæmaturia had returned and was becoming profuse. On cystoscopic examination the bladder was found normal, but blood could be seen coming from the right ureter. Suprapubic cystotomy was first performed, and later the right kidney was exposed and removed, although no lesion was found. The patient recovered and the condition was attributed to a general purpuric state.

F. Suter[5] reports the case of a woman, thirty-two years old, with an hereditary predisposition to tuberculosis, whose urine, passed without difficulty, had been turbid and bloody for a year and a half. On examination tenderness was elicited over the situation of the left kidney,without increased resistance or tumefaction. The urine contained blood corpuscles and squamous epithelial cells, but no renal elements and no tubercle bacilli. With the aid of the cystoscope the bladder was found to be normal, but bloody urine could be seen entering from the left ureter. Tumor or tuberculosis being suspected, lumbar nephrectomy was undertaken and successfully performed. The removed organ was found to be entirely normal, but the renal pelvis and the adjacent ureter were the seat of disseminated miliary telangiectasis.

[1] L'Association Française d'Urologie, Paris, 1900, p. 100.
[2] Ibid., p. 125.
[3] Ibid., p. 152.
[4] Medical News, December 7, 1901, p. 896.
[5] Centralblatt für die Krankheiten der Harn- und Sexual-Organe, 1902, Bd. xiii., Heft 1, p. 26.

A. T. Cabot[1] reports the case of a woman, forty-three years old, who had on several occasions had profuse hæmaturia, the only possible cause for which that could be found was downward displacement of the right kidney. Other measures failing to afford relief the suspected organ was exposed and restored to its proper position, and there was no further recurrence of the bleeding.

W. H. Jalland[2] relates the case of a man, thirty years old, who had for some time been suffering from pain over the right kidney, with frequent attacks of hæmaturia, and had also passed several small fragments of uric acid calculi. The pain increasing in severity, the right kidney was exposed and punctured in five or six places, but no stone could be detected. The organ was replaced, the wound healed, and there was no return of pain or of hæmaturia.

I have, for convenience of study, arranged the cases considered in this communication in tabular form. (See pages 652 and 653.)

An analysis of the 48 cases comprised in this tabulation yields the following results:

Sex. The sex is mentioned in 47—31 females, 16 males.

The condition thus appears to be more common in women than in men. The cause for this preponderance may, perhaps, be found to reside in the greater frequency of neurotic disorders in women, of displacements of the kidney, and of circulatory derangements due to constriction of the waist by clothing, or in disorders associated with pregnancy and lactation.

Age. The age of the patient is mentioned in 45 cases, the youngest being eighteen, the oldest seventy-six, the average thirty-six years. The distribution according to decades is as follows:

	Cases.
From 10 to 19 years	2
" 20 to 29 "	12
" 30 to 39 "	15
" 40 to 49 "	8
" 50 to 59 "	7
" 70 to 79 "	1

The great majority of cases—60 per cent.—are thus seen to come under observation during the most active period of life, that is, between the twentieth and the thirty-ninth year.

Kidney Affected. The bleeding came from the left kidney in 23 cases, and from the right kidney in 25 cases. This practical equality in the involvement of the two kidneys indicates that the disorder is not dependent upon local anatomical conditions.

Clinical Diagnosis. In almost all of the cases in which a diagnosis was recorded calculus or neoplasm or tuberculosis was suspected: in 1 nephritis, in 1 hæmophilia, in 1 hysteria, and in 1 angioma or angioneurosis.

[1] Boston Medical and Surgical Journal, March 6, 1902, p. 243.

[2] Lancet, May 3, 1902, p. 1280.

TABULATION OF CASES OF UNILATERAL RENAL HÆMATURIA.

Reporter.	Sex and age	Kidney affected	Clinical diagnosis.	Operation.	Morbid anatomy.	Result.	Pathological diagnosis.
Durham,	F. 43	Right	Calculus.	1. Kidney exposed; 2. Nephrectomy.	No abnormality.	Death.	
Lauenstein,	M. 47	Right	.....	Kidney exposed; pelvis opened; kidney punctured.	No abnormality.	Recovery.	
Anderson,	F. 24	Right	Calculus.	Kidney palpated, punctured.	No abnormality.	"	Neurosis.
Sabatier,	F. 30	Right	Calculous pyelitis.	Nephrotomy, nephrectomy	No abnormality.	"	Hæmaturic nephralgia.
Schede,	M. 50	Left	Calculous tuberculosis or malignant disease.	Nephrectomy	Kidney friable, anæmic, seat of petechiæ.	"	Local hæmophilia.
Senator,	F. 19	Right	Hæmophilia.	Nephrectomy	Nephritis.	"	Renal hæmophilia.
Abbe,	...	Right	.....	Decapsulation, puncture.	Gritty point at papilla of pyramid.	"	
Legueu,	M. 26	Left	.....	Decapsulation.	Kidney displaced and movable.	Death.	Idiopathic renal neuralgia.
Stavely,	F. 39	Left	.....	Nephrotomy.	No abnormality.	Recovery.	
Stavely,	F.	Left	Neoplasm.	Nephrotomy.	Nephritis.	"	
Israel,	F. 42	Left	Neoplasm.	Nephrotomy.	No abnormality.	"	
Broca,	F. 28	Right	Tuberculosis or neoplasm.	Decapsulation, palpation.	No abnormality.	"	
Picque and Reblaub,	F. 76	Left	Malignant disease.	Decapsulation, evacuation of cyst, excision of cyst wall, nephrotomy.	Cyst of kidney.	"	
Picque and Reblaub,	F. 39	Right	Neoplasm.	Kidney exposed.	No abnormality.	"	Vasomotor disorder.
Oliver,	M.	Left	.....	Kidney probed, nephrotomy.	No abnormality.	Death.	Nephritis.
Oliver,	M. 54	Right	.....	Kidney exposed.	Kidney shrivelled.	Recovery.	
Elb,	M. 22	Left	Morphinism.	Nephrectomy	No abnormality.	"	Angioneurotic hæmaturia.
Guyon,	M. 26	Right	Tuberculosis.	Nephrotomy.	No abnormality.	"	
Guyon,	F. 35	Right	Carcinoma.	Kidney exposed.	No abnormality.	"	Congestion; lactation.
De Keersmaecker,	F. 43	Left	.....	Nephrectomy	Chronic nephritis.	"	
Debaisieux,	F. 20	Left	Neoplasm or calculus.	Nephrotomy.	Minute translucent prominences in pelvis of kidney.	"	
Dandois,	F. 30	Right	.....	Nephrotomy.	Congestion.	"	Pregnancy.
Harris,	M. 50	Left	Angioma or angioneurotic hæmaturia.	Nephrotomy.	No abnormality.	"	
Genouville,	M. 51	Right	Calculus or neoplasm.	1. Decapsulation, nephrotomy; 2. Nephrectomy.	False membrane in pelvis of kidney.	"	Secondary hydronephrosis.
Genouville,	M. 35	Right	.....	Nephrotomy.	Kidney large, hyperæmic: capsular adhesions.	Recurrence.	

Reporter.	Sex and age	Kidney affected	Clinical diagnosis.	Operation.	Morbid anatomy.	Result.	Pathological diagnosis.
Demons,	F. 24	Left	.....	Nephrectomy	Sclerosis of kidney.	Recovery.	
Loumeau,	F. 32	Left	.....	Nephrotomy.	Congestion.	"	
Debersaques,	M. 38	Left	.....	Nephrotomy; sound introduced into ureter.	Congestion.	"	
Poirier,	F. 43	Right	Calculus.	Nephrectomy	Chronic nephritis.	Death.	
Pousson,	F. 23	Right	Primary renal tuberculosis or epithelioma.	Nephrotomy; nephrectomy.	Chronic nephritis.	Recovery.	
Potherat,	F. 52	Right	Neoplasm.	Nephrectomy	Chronic nephritis.	Death.	
Rovsing,	F. 21	Right	.....	Nephrotomy.	Kidney adherent, cyanotic, necrotic, thrombotic.	Recovery.	Compression by liver.
Rovsing,	F. 56	Right	.....	Nephrotomy.	Kidney displac'd, cyanotic.	"	Tight lacing.
Rovsing,	M. 47	Left	Neoplasm, or tuberculosis.	Nephrotomy.	Kidney displac'd.	"	Possibly small unobserved tuberculous focus or other lesion.
Rovsing,	F. 28	Left	Calculus.	Nephrotomy.	Kidney displac'd, pelvis dilated, ureter bent, bacteria in straight tubules	"	Kidney movable.
Myles,	F. 36	Left	.....	1. Pelvotomy, bougie introduced into ureter, puncture of kidney, nephropexy. 2. Nephrectomy.	1. Kidney movable, enlarged, congested, lobulated. 2. Myxangiomatous change in renal pelvis.	"	
Fenwick,	F. 18	Left	Hysteria or calculus.	Pelvotomy, telangiectasis removed.	Papillary telangiectasis.	Recurrence.	
Fenwick,	F. 30	Left	.....	Pelvotomy, telangiectasis removed.	Papillary telangiectasis.	Recovery.	
Pousson,	F. 29	Left	Calculus.	1. Pelvotomy. 2. Nephrectomy.	Kidney enlarged, uronephrotic, valve-like fold in pelvis.	"	Distention of kidney.
Pousson,	M. 36	Left	Primary renal tuberculosis.	Nephrectomy	Kidney enlarged, fluctuating calculus; renal tissue stretched.	"	Distention of kidney.
Albarran,	M. 53	Right	Nephritis.	Nephrotomy.	Kidney enlarged, hyperæmic, adherent; grayish nodule at base of pyramid.	"	Chronic nephritis.
Loumeau,	F. 34	Left	Primary renal tuberculosis.	Nephrectomy	.....	Death.	Uræmia.
Pasteau,	F. 44	Right	Nephropexy.	Nephropexy.	Kidney displac'd.	Recovery.	
MacGowan,	M. 35	Right	.....	Nephrectomy	No abnormality.	"	General purpuric state.
Suter,	F. 32	Left	Neoplasm or tuberculosis.	Nephrectomy	Disseminated miliary telangiectasis of renal pelvis.	"	
Cabot,	F. 43	Right	.....	Nephropexy.	Kidney displac'd.	"	
Jalland,	M. 30	Right	.....	Puncture.	No abnormality.	"	
Eshner,	F. 20	Right	Calculus.	Kidney exposed.	No abnormality.	"	

The diagnosis is exceedingly difficult and can be made only by excluding other causes of hæmaturia. That the bleeding comes from one kidney alone can be demonstrated by cystoscopic examination or ureteral catheterization or direct inspection of the vesical orifices of the ureters after cystotomy.

OPERATIVE PROCEDURE. The operation consisted in—

	Cases.
Simple exposure of the kidney, probably with palpation in	4
Exposure of the kidney, with puncture in	2
" " " with pelvotomy and puncture in	1
Nephropexy in	2
Decapsulation of the kidney in	2
" " " with puncture in	1
Nephrotomy in	14
Pelvotomy, with removal of telangiectases, in	2
Decapsulation of the kidney, with removal of a cyst, removal of the cyst wall, and nephrotomy, in	1
Nephrotomy, with probing, in	2
Nephrectomy in	10
Exposure of the kidney at a primary operation, followed by nephrectomy at a secondary operation, in	1
Nephrotomy and nephrectomy in	2
Decapsulation of the kidney, with nephrotomy at a primary operation, followed by nephrectomy at a secondary operation, in	1
Pelvotomy, with probing and puncture of the kidney and nephropexy at a primary operation, followed by nephrectomy at a secondary operation, in	1
Pelvotomy at a primary operation, followed by nephrectomy at a secondary operation, in	1

The preferable course of procedure would seem, after medicinal and other non-operative measures have failed to check the hemorrhage, to consist in exposure of the kidney, with incision of the organ itself or its pelvis or stripping of its capsule, and the removal of any local lesion, or the restoration of a displaced organ. Should the hæmaturia, nevertheless, persist, nephrectomy may be resorted to as a final expedient.

RESULT. Recovery ensued in 40 cases, death in 6, and recurrence in 2. Of course, it is possible that in some of the cases disease latent at the time of operation may have become manifest at a later date, and in others the cessation of the hæmaturia may not have been permanent. Nevertheless, the prognosis must be considered favorable with appropriate treatment.

MORBID ANATOMY. In 16 of the cases no lesion was discovered at operation, or at least was recorded, but failure in this direction does not necessarily imply absence of lesions, as in almost all of these, if not all, histological examination of tissue from the affected organ was not undertaken. Displacement or undue mobility of the kidney was present in 6 cases, renal congestion in 3, adhesions of the kidney in 2, inflammatory, degenerative, or other destructive lesions of the kidney in 11, alterations in the pelvis of the kidney in 9. It will be noted

that it is particularly in the earlier cases that the kidney is recorded as being healthy, while in almost all of the later cases structural changes are noted.

Various explanations have been suggested for the hæmaturia in the cases under consideration, as well as for the cessation of the phenomenon after simple exposure or manipulation or incision of the kidney. No doubt the cause is not the same in every case, as the evidence goes to show. In by far the larger number of cases in which histological examination has been undertaken lesions of an inflammatory character have been found. In some vascular changes or capsular adhesions have been noted. In a considerable number there has been mobility or displacement of the kidney sufficient to give rise to circulatory disturbances. In some, perhaps, lesions were present, though not appreciable to the naked eye. Only exceptionally could the kidney be considered healthy after histological examination. It is probable that none of the cases was an example of true hæmophilia. The suggestion of a vasomotor or angioneurotic condition does not seem an adequate explanation, and for the present it must be confessed that in a certain number of cases the cause of the hæmaturia, as well as its localization to one kidney, remains obscure. We are equally in the dark as to the mechanism through which the bleeding is controlled in the sequence of mere exposure, manipulation, or even incision of the kidney. Perhaps we have here an analogy with the recovery that sometimes follows abdominal section in cases of tuberculous peritonitis. It has also been shown that the symptoms of nephritis may be relieved by division or stripping of the caspule of the kidney, or puncture of the organ, probably through circulatory modifications thus brought about. A similar explanation may be applicable to the results of appropriate operation in the presence of adhesions or displacement, or mobility of the kidney.

That the kidney may be the seat of disease when thought to be healthy is shown by the demonstration made by Nicolich[1] before the meeting of the French Urological Society, October 24, 1901, of a kidney from a patient operated upon with success for the relief of hæmaturia designated essential and reported free from lesion, but which, on further examination, was found to present histological appearances of glomerulo-nephritis.

A case that is interesting, among other things, from the therapeutic standpoint has been reported by J. Passet.[2] The patient was a married woman, in whom hæmaturia set in at the menstrual period and persisted beyond. The condition was thought to be due to detachment of a papilloma of the bladder. The urine was, on examination,

[1] Annales des Maladies des Organes Genito-Urinaires, 1901, p. 1376.

[2] Centralblatt für die Krankheiten der Harn- und Sexual-Organe, 1894, v. p. 397.

found to contain only red and white blood corpuscles. The bleeding ceased after the injection of a solution of silver nitrate, but it recurred after an interval of nineteen months, following some emotional disturbance. The hæmaturia now failed to yield to treatment, and the patient declined to submit to operation. Digital examination disclosed the presence of a coarsely granular and trabeculated area on the posterior wall of the bladder. The condition of the patient became so grave that operation was insisted on. Accordingly suprapubic cystotomy was performed, but no lesion of the bladder was disclosed. On introducing a catheter into each ureter blood was seen to escape from the right. The hæmaturia ceased on the following day, without further manipulation. It returned, however, after the lapse of twenty-one months, but it ceased with rest in bed, and it had not returned eleven months later. The condition is believed to have been one of local hæmophilia.

A somewhat analogous case has been reported by Potherat.[1] The patient was a woman, thirty-three years old, who had suffered from profuse hæmaturia for four years, and presented an anæmic appearance. On examination it was thought that the kidneys were not increased in size, but rather smaller than normal. There was, however, slight pain in the right costo-vertebral angle on manipulation. On cystoscopic examination and ureteral catheterization blood was seen escaping from the right ureter. The urine contained albumin in considerable amount. Subsequent attempts at ureteral catheterization for the study of the urine from each kidney proved unsuccessful, but the hæmaturia ceased and did not recur.

In neither of these cases, it will be noted, was the suspected kidney exposed, so that no definite opinion can be formed as to whether it was diseased or not. The cases, though instances of unilateral renal hæmaturia, are, therefore, not included in the foregoing tabulation.

The following case can scarcely be considered one of unilateral renal hæmaturia, inasmuch as the hemorrhage failed to cease after the removal of the kidney suspected to be the source of the bleeding. Of course, the other kidney may have been the one at fault, but of this there is no evidence.

At a meeting of the Société de Chirurgie held June 8, 1898, Nimier[2] reported the case of a young man, seventeen years old, who suffered from hæmaturia, with remissions, for four years following an injury to the left side of the abdomen.

There had been colicky pain in the course of the left ureter, with tenderness on palpation. The urine contained numerous red blood

[1] Bulletin et Mémoires de la Société de Chirurgie de Paris, 1898, p. 634.

[2] Ibid., 1898, xxiv. p. 631; also Annales des Maladies des Organes Genito-Urinaires, 1898, p. 281.

corpuscles, a small number of leucocytes, but no bacteria or other parasites. Nothing abnormal being found on cystoscopic examination, the left kidney was exposed and found indurated at its superior pole. The organ was incised and on section presented a grayish-yellow appearance. A neoplasm being suspected the kidney was removed, but the hæmaturia persisted. On histological examination a slight degree of sclerosis of the kidney was found at one point only, with proliferation of embryonal cells.

Conclusions. There occurs occasionally, in men and women alike, mostly at middle adult life, hemorrhage from a single kidney—from either with equal frequency, in many instances in consequence of demonstrable organic disorder, and in the remainder of obscure and undetermined origin. This hæmaturia may cease after simple exposure of the kidney, or after nephropexy or nephrotomy, or in the failure of these after nephrectomy.

Note.—Since the foregoing communication was read I have come across the report of an additional case in which slight mobility of the kidney was attended with profuse hæmaturia.[1] A middle-aged woman presented herself on account of pain in the right loin, frequency of micturition, and hæmaturia. Five years previously she had been seized with pain in the right loin, associated with the presence of a small amount of blood in the urine. Her medical attendant suspected the presence of a calculus, but no conclusive evidence was discoverable. Attacks of pain recurred, and hæmaturia took place from time to time. There had been loss of weight and strength. Tenderness was present in the right loin, and the right kidney seemed larger than the left, and it moved more with respiration. The bladder was examined under anæsthesia, and was found healthy. The urine contained blood and pus cells, but no crystals, or casts, or tubercle bacilli. The right kidney was exposed, and found enlarged and congested. It was incised and explored, but no stone or obstruction or other abnormality was found. The organ was sutured in place. Recovery was uninterrupted, and there was no recurrence.

In another case hæmaturia of four years' standing was associated with chronic parenchymatous nephritis, and ceased after operation on the kidney.[2] The patient was a farmer, forty years old, who for four years had not noticed the urine to be dark in color, and an examination disclosed the presence of blood. The condition was thought to be dependent on the presence of a stone in the bladder. There was increased frequency of micturition, and the appearance was anæmic, but there had never been a chill or febrile attack, and there was no elevation of temperature

[1] R. Earle Newton. Australasian Medical Gazette, December 23, 1902, p. 622.
[2] C. H. Chetwood. Medical News, February 7, 1903, p. 256.

and no evidence of pulmonary or cardiac lesion. The urine was uniformly bloody. It contained red blood corpuscles, but no pus, no tube casts, and no tubercle bacilli. On palpation a slight amount of tenderness seemed present over the lower pole of the right kidney. The prostate gland was not enlarged, no stone could be detected in the bladder, and no lesion of the urethra discovered. On cystoscopic examination blood was seen issuing from the right ureter, while the urine from the left ureter was clear. The right kidney was, accordingly, exposed and divided, but the only abnormality found was a small indurated area on the anterior surface near the pelvis. This was incised and a small piece removed for microscopic examination. The blood disappeared from the urine in the course of three or four days, and it did not thereafter reappear. Histological study of the tissue removed disclosed the lesions of chronic parenchymatous nephritis.

BENCE JONES ALBUMOSURIA, WITH PECULIAR NERVOUS PHENOMENA.

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The attention that has been devoted to this subject during the past decade appears to warrant the recording of such cases; and while these reports have been more or less isolated—nine occurring in America—and have appeared under a variety of titles, as osteomalacia, osteosarcoma, carcinoma of the bones, lymphatic leukæmia, pernicious anæmia, myxœdema, etc., the majority, and possibly all, have been associated with new-growths of the bony skeleton, which should probably be regarded as multiple myeloma. In three examples, with a review of the literature, reported in collaboration with Dr. J. M. Anders,[1] deformities of both the long and flat bones were detected ante-mortem in one of them; in another there was considerable recent deformity at the site of the fracture of the ankle.

The patient who forms the basis for this report first came under my care two years ago, at which time she was found to be suffering from gastro-intestinal catarrh.

Mrs. L., widow, aged fifty years, housewife, and of American birth. Her family history gave nothing of interest. Had the diseases of childhood; two children, both now living, the younger a daughter, aged twenty years. There had been a tumor developing in the left breast during the past eight years, and in 1898 this breast was removed by Dr. T. S. K. Morton, who stated that the growth was a carcinoma, but up to the present time there is no perceptible return of the trouble.

There have been repeated attacks of obstinate constipation, lasting from one to five days, at which times the abdomen became hard and nodular, and there were intense abdominal pains, accompanied by paroxysmal vomiting. Vomiting without apparent cause has been a prominent feature, while both lancinating, dull, and boring pains arising in the back and pelvis and radiating to the umbilicus and pubes have comprised the most distressing symptoms during the past six months. There has often been a feeling of "giving away" of the left leg and the bones of the left pelvis while walking or when ascending the stairs. These pains were agonizing, compelling her to cling to the nearest object for support.

Within the last five years her weight has been reduced from 185 pounds to 95 pounds; the greater portion of this loss has taken place during the past year, however. Together with the rapid loss of flesh and strength there developed œdema beneath the eyes, pallor of the skin and mucous surfaces, frequent attacks of urticaria, and cutaneous abscesses of the scalp and dorsal surface of the chest.

Early in January, 1902, she received a fall, inflicting a lacerated wound of the occiput and rather severe contusion of the left shoulder. It was not until six weeks later that the peculiar urinary phenomenon (albumosuria) was detected.

Neuralgic pains in the left shoulder which radiated to the left hand were most annoying, and often prevented sleep. There were, at times, numbness and a feeling of "pins and needles" in the left arm and hand. The left thigh, leg, and foot have also been painful, and at night these pains became cramp-like, causing muscular contraction. The great and adjacent toes of the left foot were anæsthetic to deep prick of a pin, and sensation was impaired over the inner surface of the foot and leg. Over these regions there was inability to distinguish between hot and cold. There was no apparent atrophy of either the foot or leg, and the muscles reacted normally. The left knee-jerk and the plantar reflex were decidedly increased, and ankle clonus was marked. Other reflexes normal.

The heart's action was regular at 70 beats per minute; no murmurs were audible, but there appeared to be a lack of muscular element with the first sound. The radial and temporal arteries were atheromatous. Lungs and the abdominal viscera normal.

There had been failing of vision during the past year, and I am privileged through the courtesy of Dr. L. Webster Fox to add his report of an ophthalmoscopic study: "The right eye shows slight diffused retinitis, with possibly posterior vitreous changes, which are so slight, however, that I cannot differentiate between the posterior part of the vitreous and that of the retina. I am inclined to believe this haziness to be retinitis. There is marked sclerosis of the blood-vessels, the arteries more pronounced than the veins. There does not seem to be the normal difference between the arteries and veins. The optic nerve is hazy, although I can find no deposits of albuminoids in the retina, and there are no hemorrhages. The left eye shows the same appearance as the right. The pupils respond to light sluggishly. The lessened vision is due to interference with the media."

The urine was first noted to give the reaction for the Bence Jones body March 12, 1902. Repeated examinations were made during the

following month, all of which showed this substance to be present. More recently, however, the results of a number of examinations have been negative; while those of others where the urine was collected during the same week have given positive reactions, which places this case in the category of those reported by Kahler,[2] and by Kuhne and Stokvis,[3] where the albumosuria was intermittent. The urine was acid in reaction, specific gravity 1008 to 1012, light amber or water color, often turbid, and the twenty-four hours' product equalled 1200 c.c. A trace of serum albumin was always present. Microscopically, the sediment contained epithelial cells, amorphous urates, and a few leucocytes. No renal casts were seen.

The methods employed for the study of Bence Jones albumose were those suggested by Henry Bence Jones,[4] Huppart,[5] Matthes,[6] Milroy,[7] paper and Magnus-Levy,[8] and have been considered in a previous paper upon this subject;[1] and Dr. Simon has thoroughly considered these reactions in a contribution to this JOURNAL for May, 1902.

During the past year there has been decided pallor, though many of the general symptoms commonly known to accompany such blood impoverishment were wanting. An examination of the blood July 14, 1902, gave: Red cells, 4,430,000 per c.mm.; white cells, 8600; hæmoglobin, 39 per cent. The differential leucocyte count showed: Polymorphonuclear cells, 39 per cent.; large mononuclear, 15.25; large lymphocytes, 20; small lymphocytes, 21.5; eosinophiles, 2.25; transitionals, 2. Other examinations gave results which differed but slightly from the above except in the quantity of hæmoglobin, which reached 55 per cent. on one occasion. The erythrocytes were always found to be above 4,000,000 and the leucocytes below 8600. Here the anæmia appears to be of a chlorotic character, the hæmoglobin alone suffering loss. Stained specimens displayed a high grade of poikilocytosis, and microcytes and macrocytes were occasional findings. No nucleated red cells were detected. The pronounced increase in the mononuclear leucocytes to 56.75 per cent., with a reduction of the polymorphonuclear elements to 39 per cent., appears worthy of special mention.

Albumosuria developed after the removal of a rodent cancer from the nose, in the case reported by Bradshaw and Warrington.[9] It appears difficult to show, in my case, that the albumosuria has any relation whatever to the cancerous growth removed from the breast four years previously.

Senator,[10] in 1897, called attention to certain nervous phenomena appearing with albumosuria. His patient, a female, aged thirty-six years, suffered from paralysis of the hypoglossal nerves, paresis of the arytenoideus, and anæsthesia throughout the course of distribution of the trigeminal nerve.

Fitz[11] observed the case of a female, aged forty-nine years, who complained of a sense of numbness in the right heel, knee, and fingers of the right hand. The teeth were painful, and changes in the voice, tongue, skin, and its appendages were also present. Fitz regards this case as one of myxœdema with albumosuria.

James H. Wright[12] has reported the case of a male, aged fifty-four years, in whom there were numbness of the feet, double vision, and strabismus. The knee-jerks were exaggerated and ankle clonus pronounced.

L. P. Hamburger,[13] in the first case reported by himself, refers to repeated attacks of facial neuralgia. The patient was a female, aged forty-nine years.

A. Raschkes'[14] case was that of a female, aged forty years. The initial symptom was momentary, cramp-like pains in the right foot.

Case I. of the series reported with Dr. Anders suffered continuously from cranial and facial neuralgia. Case II. often referred to a tingling sensation of both the hands and feet and of neuralgic pains in the lower limbs; while in Case III. there was paralysis of the left side of the face. In reviewing the records of cases furnished by the literature, cephalalgia and neuralgia are among the most constant of symptoms, yet in the case herein reported cerebral pains have been infrequent.

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ON A NEW METHOD FOR THE APPLICATION OF WIDAL'S TEST FOR THE DIAGNOSIS OF TYPHOID FEVER.

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Of the many technical applications of the Widal reaction, the most popular as well as the most practical is the dried-blood method of the

late Dr. Wyatt Johnson; and the extension of his method which I am about to describe will, it seems to me, tend to add to its utility as well as to its accuracy. The technique is very simple. A loop from the feces of the suspected case is smeared upon the surface of an agar slant in a prepared tube and sent to the laboratory just as diphtheria cultures are prepared. In the absence of an agar tube a small piece of paper soiled with the feces may be sent in a tightly closed bottle. From this first specimen one or more bouillon cultures are prepared. The bouillon must react from 1 to 2 per cent. *alkaline* with the $\frac{N}{10}$ acid, using phenolphthalein as the indicator. The infected bouillon is now incubated at the usual temperature for twelve hours, when we are ready to make the examination. A sample of the blood is taken at the same time the specimen of the feces is procured. This is mixed with the bouillon culture by the usual procedure and placed upon the stage of the microscope. If now there is sufficient agglutinative material present the typhoid bacilli (if they exist in the culture) will very shortly form clumps in the fields, which will be observed full of colon bacilli in active motion; and if this reaction does occur we can, of course, safely say that the case has advanced at least to the second week of the disease. Should no reaction take place, another sample of the bouillon culture is tested with the blood from an advanced case of typhoid fever, the agglutinative power of which has been tested by the ordinary method, with a pure culture of the bacillus of Eberth. Indeed, it is necessary for the proper use of this test to keep in stock a number of specimens of blood from well-marked typhoid cases. These can be kept in a dry place, and they retain their power to produce a reaction with a pure culture, probably indefinitely. With this blood, if the feces contain any typhoid bacilli, a positive and distinct reaction will shortly occur, the clumps of typhoid bacilli being more or less numerous according to the number of typhoid organisms present, while the still motile colon bacilli occupy the rest of the field, and are seen to be in active motion. This indicates that the case is one of typhoid fever, and that the disease is in the early stage, at least from the middle to the end of the first week. By means of this simple method we are enabled, in my opinion, to make an accurate diagnosis in the early stages of the disease when the other symptoms may be more or less masked, and thus remove many elements of doubt in a suspicious case.

On the other hand, we are enabled to state that the patient has advanced at least into the second week of the disease, or beyond the seventh day if his own blood produces a positive reaction by my method. One might easily conceive, of course, that rare condition of a second attack within a period too brief to destroy the agglutinative reaction of the blood, the result of the *first* attack of the disease; but such an exception must be extremely rare, and would produce much

more chance for error by the ordinary application of the Widal test. I am well acquainted with the fact that certain observers claim that they have been unable to discover the presence of the typhoid bacillus in the feces previous to the eleventh day of the disease; but from the distinct reactions which I have obtained by my method (which, almost without exception, in the cases in which I have used it has produced clumping in the very early stages of the disease), and which, by this method alone, I have been enabled to diagnose typhoid fever I am certain that the bacillus of the disease *is* present in the feces quite a time before the outbreak of the symptoms.

In thirty-five tests which I have made within the past six months of cases in the earlier stages of the disease, every case that gave a positive reaction by this method turned out to be typhoid fever, while in a large number of other tests from which *no* reaction was obtained I do not know of one in which this method has given even a *doubtful* reaction.

If it is true that the agglutinative material in typhoid blood reacts by producing clumping with the typhoid bacillus, and does not give a reaction with the colon bacillus, then there is no reason why this method should not prove of great utility in the bacteriological laboratory as well as to the general profession.

I have avoided, in this short notice, commenting upon the many sources of error which have in no small degree tended to affect the accuracy as well as the utility of the Widal test. While I am conscious of the fact that my extension of the Widal method has only been tested upon a limited number of cases, still it has been productive of such good results, and is so full of possibility that I have felt it incumbent upon me to place it before the profession.

LATE SYSTOLIC MITRAL MURMURS.

By J. N. Hall, M.D.,
of Denver, Col.

In The American Journal of the Medical Sciences for September, 1892, Griffith reported three cases in which the murmur of mitral regurgitation was heard after the apex beat and the first sound of the heart, instead of synchronously with and following them. In the *Medical News* for October 20, 1894, I reported a similar case, but with a different explanation. Since that time I have heard many such late murmurs of mitral insufficiency, and Griffith has told me that he encounters them frequently. Other physicians have occasionally reported their occurrence, but no generally accepted explanation of the late development of the murmur has been advanced.

I will here briefly report a typical case, as a basis for a closer study of the peculiarity of the murmur.

Mrs. A. N., aged thirty-five years, German, in Colorado four years; family history negative. She has suffered an attack of acute rheumatism, but has been well otherwise since childhood. Her four labors have been uneventful. She complained of rheumatic pains in the wrists, of slight swelling of the feet and the lower eyelids, of dyspnœa upon exertion, with occasional nose-bleed.

Her pulse was regular, 60 per minute, of good tension. Temperature normal. Tongue slightly coated. Feet and eyelids slightly œdematous. Examination otherwise negative, excepting as regards the heart. By percussion this organ was enlarged to just beyond the nipple line at the left, and slightly to the right. The apex beat was just outside the line mentioned, in the left space. In the mitral area was heard a murmur transmitted three inches to the left, and slightly in other directions, but most distinct just under the nipple, beginning abruptly after the occurrence of the apex beat and first cardiac sound, and ceasing just before the second sound. No other murmurs. No reduplication nor accentuation of the basic sounds. No anæmic hum in the neck, or other signs of anæmia. The murmur was of the blowing character commonly found in this location.

The urine was acid in reaction, high in color, specific gravity 1029, no albumin or sugar.

Dr. Henry Sewall kindly saw her with me, and we found the condition as at first examination. With the differential stethoscope, one bell applied over the place of the murmur, and the other over the lower end of the sternum, we were able to note very easily the difference in time between the apex beat and the beginning of the murmur. Dr. Sewall, who has done much original work with the instrument in question, both in clinical and in physiological study of the heart's action, stated that he could distinguish a cardiac contraction synchronous with the beginning of a murmur, and, of course, later than the apex beat. At the meeting of the Colorado State Medical Society in June, 1896, the case was exhibited, and many physicians examined the heart. Apparently owing to the excitement its action was peculiarly forcible, and hence the characteristics of the murmur were very distinctly shown. Drs. Dennison, Whitney, Hershey, Packard, and many others examined the case, under favorable circumstances, and there was no discrepancy as to the facts, viz., that the area of cardiac dulness and the time of the murmur were as stated, and that the latter was transmitted to the left. There was much discussion as to the manner of origin of the murmur. All agreed that the mitral valve was incompetent.

Griffith's explanation of the peculiar time of this murmur is, that it is the ordinary sound of mitral leakage, with the exception that in its earlier stages the regurgitant current gives rise to no vibrations perceptible to the human ear as sound. I see no reason why this explanation may not apply in certain cases. After considerable study, however, I am satisfied that the explanation offered with my first reported case more nearly meets all the difficulties we encounter, in these cases,

than any other. That explanation was as follows, viz., that the first cardiac sound and the apex beat were due to the contraction of the right ventricle and closure of the tricuspid valve, the latter being presumably free from disease; and that the murmur was caused by regurgitation through a diseased mitral valve, and was later in time than the apex beat because of a tardy contraction of the left ventricle. In other words, if the mitral valve had been normal, so that no leakage could have occurred, we should have had a case of reduplication of the first sound, other conditions remaining the same.

If this particular case is to be explained upon the theory of Griffith, the murmur should have begun gradually, resembling, in its mode of beginning, the presystolic murmur of mitral stenosis. In my opinion a murmur beginning with a sharp puff must depend upon some sudden change in the hydraulic conditions within the heart, not upon a continuous regurgitant current, giving rise at a certain point to audible vibrations, which instantly reach their fullest intensity, all of which conditions would be necessary for a satisfactory explanation according to the theory mentioned. I conceive that a sharply beginning murmur must take origin in a sudden contraction of the walls of the cavity of the heart involved, or in a sudden yielding of the valve from inability to withstand the pressure of the contained blood. We should mention, however, that in none of the cases heretofore recorded has this sharp beginning of the murmur been especially noted, although I have recognized it probably a dozen times since.

It has long been known that reduplication of the basic sounds of the heart is frequent in mitral disease, and certain French authorities lay great stress upon this phenomenon in the diagnosis, especially of mitral stenosis. Most clinicians, I believe, recognize this reduplication, and accept the usual physiological explanation, viz., that it depends upon asynchronous contraction of the two ventricles. The right ventricle, owing to the increased tension in the pulmonic arterial system, dependent upon the mitral disease, anticipates the left by an instant. Thus we find in these very cases of mitral insufficiency we should *a priori* expect such asynchronism.

In a proportion of these cases we should also expect to find basic reduplication as a complement to the asynchronous ventricular contraction, since contractions beginning at different times might be expected to end likewise. Dr. Sewall has called attention to the fact that all grades of variation from the normal of the basic sound of the heart, from a simple indistinctness in the single sound, to distinct doubling may be detected. Since my attention was drawn to this point by him I have frequently noted the presence of a splitting of the second sound in the cases of late mitral murmur. It was easily recognized by both of us in one instance which I saw with Sewall a few years ago.

We have implied above that such a murmur might arise from the yielding of a valve after it had successfully withstood the pressure of the first part of the systole. We may conceive that disease of the papillary muscle supporting a segment of the mitral valve might so weaken it that it should be unable to stand the prolonged strain of the systole, although able to close the orifice by its contraction for an instant. Because of the brief duration of the maximum intraventricular pressure, however, this condition could not probably explain very late systolic murmurs, for if the valve did not yield during the time of highest pressure it would be unlikely to do so later. I do not, however, believe that this explanation applies to the case in hand.

Roy and Adami have shown that the final act in ventricular contraction is a pulling in of the auriculo-ventricular curtains by contraction of the papillary muscles. This causes a perceptible increase in the intra-ventricular pressure. If we may conceive that this pressure, in a given case, before their contraction, was so great that the action of the muscles, perhaps weakened by disease, was delayed an instant, and that, with the contraction, owing to dilatation of the ventricle and consequent spread of the base of support, the valve curtains were pulled apart, permitting regurgitation, we should have a beautiful theory of the origin of the late mitral systolic murmur.

I conclude, then, that in general we may explain these murmurs by asynchronous ventricular contraction. This theory is supported by the recognized frequency of such abnormal action of the heart in those cases in which the pressure in either system is abnormally increased. The right ventricle anticipates the contraction of the left in mitral disease, as we have seen, while the converse probably occurs in interstitial nephritis and other diseases raising the systemic tension above the normal. Confirming this hypothesis we have the recognition of basic reduplication in certain of the cases studied. I admit the plausibility in some circumstances of Griffith's explanation, and the possibility of the above-mentioned anomalous action of the papillary muscles in others.

CONCERNING THE ROLE OF INTRACELLULAR CATALYTIC PROCESSES IN THE PATHOGENESIS OF MALIGNANT NEOPLASMS.

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It is now accepted as one of the truths of physiology, as well as pathology, that the cells of the mammalian organism may change their form, and even at times their structure, during their existence. Physi-

ologically, they may change their forms under the influence of age, and according to many extrinsic and intrinsic influences to which they are subjected. It is often impossible to draw sharp lines of demarcation between that which is normal and that which is abnormal in such changes. Virchow expressed himself in the words that in reality there is no distinct line of demarcation between "physiological and pathological processes, and that the latter are only physiological processes which take place under difficult conditions." Cancer pathogenesis may accordingly be looked upon, in part at least, as a problem of growth of cells under difficult conditions, and in that case we have a right to expect that the solution of this problem may be aided by the adaptation and application of recent discoveries in physical chemistry to the pathology of cell growth, just as physical chemistry by its revelations concerning osmosis and the ionic theory has thrown light upon normal cell growth.

We have learned to look upon the individual cell as representing in itself a highly complicated system of organized parts, the latter standing in most intimate co-relation with each other. The cell may be conceived as representing on a small scale that which the entire cell state is on a grand scale, *i. e.*, a unity, a specific system of organized parts. Shall we seek the cause of malignant neoplasms, conditions of cell anarchy, caricatures of normal developmental processes, within or without the cell? This question separates all hypotheses concerning the etiology of malignant neoplasms into two great groups:

First, those assigning the cause of cancer to qualities inherent in the cells themselves. Secondly, those assigning the etiology of cancer to the action of some extraneous poison, particularly to the influence of micro-organisms. Although the latter theory may logically include the effect of toxins, even those not of bacterial origin, these two great groups may be concisely designated as, first, the histogenetic, and second, the parasitic theory, on the origin of cancer.

It is not my intention to discuss in this report the relative merits and demerits of these two groups of hypotheses. These matters are set forth in the various works on pathology, but most forcibly, perhaps, in the work of Professor David von Hansemann, *Die Mikroskopische Diagnose der Bosartigen Geschwülste.* Also in the work by Lubarsch, *Zur Lehre von den Geschwülsten*, in Ribbert's work, *Lehrbuch der allgemeinen Pathologie*, and in various editions of Lubarsch and Ostertag's *Ergebuisse d. Pathologie.* Hansemann, Ribbert, and Lubarsch are opposed to the parasitic theory, and by far the greater number of prominent German pathologists, while they are non-committal, have not given support to it. Recent American research work by R. B. Greenough, and Edward H. Nichols, published under the auspices of the Harvard University Cancer Commission, in the *Journal of Medical*

Research, 1902, vol. ii., invalidate the parasitic theory. On the other hand, the histogenetic theories, as examples of which we may mention those of Thiersch, "Der epithelial Krebs," Leipzig, 1865; Cohnheim, (*Allgemeine Pathologie*, Bd. i., S. 723) and Ribbert (l. c.) have the advantage that they cannot be controverted at all, being hypotheses pure and simple, without experimental foundation, so that they cannot be tested experimentally. The only excuse for the formulation of an hypothesis is that it gives the incentive to experimental investigation, and the formulation of inquiries into the nature of the thing discussed; and an hypothesis that does not permit of this has thrown no light on the subject to be solved, but simply side-tracked it. Thiersch conceived that the connective tissue might become weakened by disease or old age, and thereafter the epithelial tissues gain the supremacy and penetrate into the depths of other tissues. This theory does not explain the occurrence of cancer in young people, and cannot be tested experimentally.

Cohnheim conceived the cause of malignant neoplasms to be the supposed existence of congenital embryonal cells, which have remained latent in different tissues of the body. This theory does not explain why such undifferentiated embryonal cells, if they really occur, should suddenly begin to proliferate in an unrestricted manner.

This theory of Cohnheim has not become more probable by the discovery of unutilized segmentation cells of the frog by Roux,[1] who observed that in this animal, cells occurred which were not utilized, and were surrounded by growths of other cells. Barfurth observed the disruption and subsequent continued growth of a segmented portion of the exoderm. With regard to the mixed tumors it is very probable, however, that they can arise from disrupted embryonal germinal cells. Ribbert is of the opinion that this is particularly the case in sarcomas occurring in the very young.[2] Many of the tumors, particularly malignant tumors (glioma, teratoma, myosarcoma), would receive a satisfactory explanation of their histogenesis from the assumption that they grow from pre-existing dislodged embryonal cells. This is particularly true of tumors like carcinoma of the kidney developed from dislodged portions of the adrenal bodies. Ribbert assumes that these grow from portions of the adrenals which have been disrupted in an embryological state and continued to live in the substance of the kidneys. Such embryonal germinal cells may remain quiescent in the kidney parenchyma without forming a tumor, but under certain conditions which are not as yet thoroughly understood (Ribbert mentions hyperæmia), such cells undergo a rapid and progressive growth and multiplication. At first this is apparently a benign growth; it is well circumscribed and limited. But when it strikes a vessel and causes its

[1] Anatomisches Heft, I. Abth., Heft 9.

[2] Loc. cit., p. 606.

wall to atrophy by pressure, it proliferates into the vascular lumen and may even cause metastases. The important point to bear in mind in the case of this tumor is that there are precursory stages which are not carcinomatous, and that they may persist in this benign state indefinitely. Evidently some additional tumor producing agency is necessary here to convert the benign growth from dislodgement of adrenal cells into the parenchyma of the kidney into a malignant growth. It shall be our duty in the following to approach a solution of this question, whether or not an additional tumor producing agency is necessary to impart the character of malignancy to cells already in a state of proliferation.

Metaplasia. The transformations in form and structure which cells may undergo are important for the understanding of normal and pathological cell growth. Evidently if cells can change their specific structure and replace it by a different structure, which is, however, definitely differentiated or undifferentiated, it is not necessary to assume with Ribbert, that in all cases of mixed tumors we are dealing with disrupted or dislodged embryonal cells, as the starting point. Lubarsch's study of metaplasia suggests the possibility of the derivation of such tumors from metaplastic cells.

The *supposed participation of muscle, liver, cartilage and lymph gland cells* in the architecture of carcinoma metastases[1] are not genuine metaplasia—*i. e., transformation meaning the replacement of specific cell or tissue structure by other definitely differentiated structure of the same kind of tissue,* but they represent what Lubarsch cells pseudo-metaplasia, *i. e.*, the histological "cell accommodations" and "variations" of Hansemann—these are mere changes of form, not of structure. Naturally if the actual participation of the liver cells, etc., in carcinoma metastases derived from an original growth the stomach could be demonstrated, it would be a point gained for the advocates of the theory of infection for malignant neoplasms, but thus far their observations are cases of pseudo-metaplasia.

Lubarsch distinguishes three types of cell changes:

1. Pseudo-metaplasia—change in form but not of structure.

2. Metaplasia—structure transformation—replacement of specific cell or tissue structure by the different kinds of structure, but which is definitely differentiated and derived from the same type of tissue.

3. Undifferentiation—transformation of definitely differentiated cells into undifferentiated. Of this there are two types:

(*a*) Transient or physiological undifferentiation, occurring during progress of indirect cell division, during which typical structure is temporarily dissolved.

[1] Rindfleisch, Klebs, Gussenbauer, von Leyden, XX. Verhandl. d. Congress f. i. Med.

(*b*) Pathological (permanent) undifferentiation which always leads to death of cells by degeneration or atrophy.[1]

Ribbert seeks the cause of carcinoma in an inflammatory proliferation, which disrupts the cell from its physiological connection. The cause of the unrestricted growth of the cell is the removal of resistance to growth in the environment caused by the inflammation. This theory does not explain why a carcinoma does not occur in every instance where an inflammation disrupts cells from their normal environment, and why carcinomas actually develop in the absence of every evidence of inflammation. It is seen that all of these theories have some resemblance. They all attribute the malignant neoplasm to some undefined power of growth within the cell and differ only in regard to the reasons assigned to this power of growth.

A fourth theory, which is that of Hansemann, does not concern the etiology of malignant neoplasms, but only their morphology and physiology. His conception is expressed in the word "anaplasia." Hansemann first used the word "anaplasia" in 1890,[2] from *ἀνα*, backward, and *πλάσσειν*, to build. He understands by it a condition in which cells have lost in part their specificity, have become "entdifferenzirt," so that they have acquired the property of independent existence, have lost what he calls "altruismus." He conceives that this anaplasia is brought about by abnormal, especially unsymmetrical, mitoses, and that some of the "idioplasm"[3] is thereby lost, while idioplasm which had previously been in the background now comes to the front.

Difficulties in the Way of the Parasitic Theory of Cancer. Above all we must recollect that the controlling histological elements in carcinomas are the connective tissue and the epithelial cells. These cells are the element which cause the tumor by their multiplication and advancement, and generate the metastases by their proliferation in other organs. We do not find such a phenomenon in the parasitic diseases. In all parasitic diseases it is the micro-organisms which transfer the diseases and then make a new inflammatory focus out of the elements and cells of the newly infected organ. In a parasitic disease the tissues of the newly infected organ itself compose the inflammatory

[1] Benecke's "Kataplasia"—Hansemann's "Anaplasia." For fuller account see O. Lubarsch, Arbeiten a. d. Anat. Abtheilung, d. kgl. Hyg. Instit., Posen, S. 209, 1901.

[2] Virchow's Archiv., Bd. cxiv., p. 321.

[3] Idioplasm. In biology, a term introduced by Nägeli for a special hereditary reproductive substance not contained in the body of the cell, but in the chromosomes of the nucleus, controlling and determining the actual characters of the particular cell, and also those of all its descendants. Each idioplasm is composed of several or many *ids*, which are capable of growth and multiplication by division; although much smaller in bulk than the rest of the living substance of the cell or body (trophoplasm), idioplasm is the active element in the process of formation, and determines the detailed construction of the trophoplasm, which is the passive element.

tumor. In cancer the cells of the secondarily infected organ never participate in the metastasis, but this is composed exclusively of the cells of the organ primarily diseased. A primary cylindrical carcinoma of the stomach, when it causes a metastasis in the liver, never infects the cells of the liver, but the metastasis is composed of cylindrical stomach cells, or glandular epithelium from the mucosa of the stomach. This is true of other metastases. In no infectious disease do we find that cells from the primary focus of inflammation are driven about, nor do such cells of infectious diseases cause characteristic new-growths histologically like themselves in other organs.

1. The parasites must live within the cell, and yet not injure it, in order to make the parasitic theory harmonize with the well-ascertained morphological facts concerning cancer proliferation. We must assume, then, a kind of symbiosis of parasite and cell. At the same time they must be able to bring into disorder the various finer cell parts already considered, in order that the incentive to cell proliferation shall be present. Whether such parasiticism is possible is doubtful.

2. As the unrestricted proliferation of the cells, as well as the power to form metastases, is ascribed to the presence of the parasites within the cells, it is necessary to assume that every cell contains a parasite, and that the parasite multiplies as rapidly as the cell, in order that each new cell shall receive its parasite. If the parasites do not divide in the identical moment that the cell divides, cells will eventually arise which contain no parasites, and, therefore, have no abnormal properties in the sense of the adherents of this theory. This condition necessitates that the cycle of development of the parasite should coincide with the rate of multiplication of the proliferating cells.

3. The best evidence points to the conclusion that transplantation of malignant neoplasms is successful only among animals of the same species. A parasitic disease, however, if we are permitted to draw inferences from the well-known infectious diseases, should be transferable from one species to another.

4. Primary carcinomas rarely occur in multiplies; only in exceptional cases of epithelioma of the skin has this been reported. Typical congenital malignant neoplasms (rhabdo-myosarcoma of the kidney, glioma of the retina) have been reported in children whose parents were not affected with malignant neoplasms.

5. The cells of organs invaded by cancerous metastases do not participate in the secondary growths. The metastases, with few exceptions, represent the cell type of the mother carcinoma.

6. Cells of a different type, then, being only exceptionally involved in the metastases, it is necessary to assume that every kind of cancer must have a special species of cancer parasite, which would not be capable of causing cells of another type to proliferate in a cancerous

manner. A pavement epithelial cell of the œsophagus, for instance, when it causes a metastasis in the stomach, produces a neoplasm composed of pavement epithelium; never cylindrical cell growth or an adenocarcinoma—structures which are found in the normal gastric mucosa.

Attempts at Experimental Production of Carcinoma. The special object of this report is to communicate in abstract a series of researches or efforts aiming at an experimental production of carcinoma of the stomach. This organ is more than all other organs in the body fitted for a study of cancer because it is more frequently invaded by this disease than any other organ or tissue in the body.[1] Not only this, but it is the only organ of which it is definitely known that a benign lesion, the peptic or gastric ulcer, may exist as such for months or even years and then can undergo changes transforming it into a typical malignant neoplasm. The scientific value of any series of investigations on cancer will depend very much upon the experience and familiarity of the investigation with the architecture and pathological physiology of these growths. It is for this reason chiefly that I confined my experimental studies to the adenocarcinoma of the stomach, believing that I could not be misled in confusing this characteristic growth with any of the other neoplasms of the stomach, or with simple inflammatory tumor. (See Hemmeter, *Diseases of the Stomach*, 3d edition, p. 527 to 586, on "Malignant Tumors of the Stomach.")

Gastric carcinoma may develop from the oxyntic or parietal cells (gland cells) of the peptic ducts, when they constitute the adenocarcinomas; but they may also arise from the cylindrical epithelium of the vestibules, and then they are termed cylindrical cell carcinomas; and finally, they may develop from the mucous glands; if the adenocarcinoma is restricted to the mucosa and grows outward, the stroma is composed of newly-formed connective tissue—if the carcinoma grows in the main muscular layer the stroma may be muscular tissue.

In 1898 I began with experiments attempting the transplantation of pieces of adenocarcinoma from the human stomach into the stomachs of dogs, cats, and guinea-pigs. I have a record of forty-two such attempts, but in not one case have I succeeded in successfully transplanting a piece of human concer of the stomach into the stomachs of any of these animals.[2]

In the *Journal of Medical Research*, vol. vi., No. 1, and vol. viii., No. 1, Dr. Leo Loeb describes the transplantation of tumors (sarcoma)

[1] The literature and statistics on this subject will be found compiled in a volume by Behla, "Die Carcinomlitteratur" (up to 1900), pages 244 and 248.

[2] The literature on transplantation of cancer from man to animals is compiled in "Ueber die Aetiologie des Carcinoms," by Gustav Fütterer, Wiesbaden, 1901. It appears from this compilation that 11 experimenters claimed to have had successful transplantations, but 19 others had negative results. A number of other transplantations are mentioned and criticised in Hansemann's work, loc. cit., p. 174.

through forty generations respectively of rats of different age and sex. In all cases a sarcoma was produced, and the details of the growth and generative changes of the cells were preserved. Even certain limits of variability in the cells were also preserved. Dr. Loeb assumes it to be a well-known fact that transplantation of cells[1] into animals of different species are usually unsuccessful, and this may account for the impossibility of producing a tumor in another species. The sarcoma which he found in the connective tissue of the parathyroid could never be successfully transplanted into any other species of animals. Guinea-pigs, animals so susceptible to tuberculosis of different origin, remained absolutely unaffected by these tumors. He suggests that certainly none of the ordinary micro-organisms can be the cause of these new-growths, of which there was no doubt that they were true sarcomata.[2]

In a more recent contribution, Mayet[3] reports transplantation experiments, in which he introduced pieces of human cancer into animals subcutaneously, or by rubbing up pieces of human carcinoma with sterile bouillon, and injected the resulting emulsion into the peritoneal cavity, or into the circulation of animals. Most frequently, however, he injected a glycerin extract of human cancer tissue, aseptically macerated, or a filtrate obtained by filtering such crushed tissue through a Pasteur filter or an asbestos filter. Previously, the animals used received cantharidin injections, with which he aimed to produce transitory nephritis and so to predispose the kidneys to the development of cancer nodules. Mayet experimented on dogs, rabbits, and white rats. He admits that his experiments on dogs and rabbits were unsuccessful, but claims that he succeeded in certainly producing cancer lesions in three white rats out of fifty-three of these animals experimented upon. These alleged successful cases he claimed were produced by the glycerin extracts or filtrates from human carcinoma. A critical study of Mayet's paper leads one to be especially skeptical concerning his claim of having produced a genuine carcinoma in this manner. He does not describe the typical architecture of a carcinoma, but speaks of epithelial cancerous lesions.

An interesting series of experiments on tumor transplantations and inoculation is described by Dr. M. Herzog.[4] The original animal which Herzog used was a descendant of the white rat from which L. Loeb[5] derived his sarcoma. The growth was a vascular cystic sarcoma of the thyroid in a rat. Over fifty successful transplantations were made in the

[1] The literature on the transplantation of cancer cells from animals to animals is compiled in the work of Fütterer, Behla, Hansemann.

[2] Loc. cit., p. 49.

[3] "Production du Cancer chez les Rats blancs Introduction dans leurs Economies des Substances constituantes des Tumeures malignes de l'Homme?" Gaz. hebdom. de Medic. et de Chir., January 19, 1902, No. 6, p. 64.

[4] Journal of Medical Research, vol. viii., No. 1, p. 74.

[5] Loc. cit.

same species of animal, and these extended over eight tumor generations. In the inoculation experiment of Herzog, pieces of non-infected sarcoma were ground up in a sterile mortar with sterile quartz sand and silicon powder. The tissues were ground up with physiological salt solution—the emulsion so prepared filtered through a Pasteur filter, and the filtrate so prepared inoculated into culture tubes, showing it to be free from micro-organisms. Several cubic centimetres of this filtrate were injected into the abdominal cavity of rats—not a single one of the rats so treated developed a tumor. Some were killed and examined, and the findings were absolutely negative. Thus far Herzog's investigations are clear and instructive; but further on he mentions the possibility of ultra-microscopic organisms, too small to be seen even by the aid of our best optical instruments. He claims that bovine pest can be propagated by filtrate through a Pasteur filter, and that the work of Nicolle and Abdil Beyer gives evidence that the cause of this disease must be a living organism which can pass through a Pasteur filter. I am not sure that the work of Nicolle and Abdil Beyer justifies such a conclusion.[1]

I have given these previous experiments such detail because they express in the work and words of others much of the work and experiment which I have made personally, yet never published. I have also prepared a sterile filtrate of human carcinoma of the stomach, exactly in the manner as described by Herzog, and injected it into the stomach tissue of dogs, cats, and rabbits, but never succeeded in causing a gastric malignant neoplasm in these animals by this process.

It is a well-known fact of pathology that the human gastric or peptic ulcer may become transformed into an adenocarcinoma, apparently spontaneously. This process has been described in a classical investigation by Hauser.[2]

In 1900 I paid a visit to Professor Hauser's laboratory at the University of Erlangen, and was fortunate enough to see some of his original preparations and sections. I have also had a rather exceptional clinical experience with cases of gastric ulcer in the human being, which I had studied, in one case, for over two years, during which it presented the typical clinical history of gastric ulcer. Then followed the clinical history of gastric carcinoma and death.[3] Naturally, the question arose in my mind, "*If gastric ulcers could be produced experimentally in animals, their transition into possible adenocarcinoma might be studied at*

[1] As far as I know the experiments of L. Loeb and M. Herzog have not been confirmed by others, nor am I in a position to judge whether the neoplasms they claim to have produced were genuine sarcomas.

[2] Das chronische Magengeschwür, sein Verharbungs-Process und die Beziehung zur Entwickelung des Magencarcinoms," Leipzig, 1883; and "Das Cylinderepithelcarcinom des Magens und des Dickdarms, Jena, 1890. See, also, New York Medical Record, 1897, vol. lii. p. 365; also, Hemmeter, "Diseases of the Stomach," third edition, p. 560.

[3] See Hemmeter, New York Medical Record, 1897.

will, or the transformation into adenocarcinoma might be attempted by the transplantation of malignant neoplasms derived from other animals of the same species, or by the injection of sterilized filtrate of ground-up adenocarcinoma of other animals of the same species into the tissues surrounding the edge of the ulcer."

Among the causes that are definitely ascertained as contributing to the bringing about of gastric ulcer are especially three:[1] first, impaired vitality or injury to the mucosa of the stomach; second, hyperacidity or supersecretion of gastric juice containing an excess of HCl, and proteolytic ferments; third, an altered or impaired state of the blood.

All three of these factors may be produced artificially, and when we do produce them in the laboratory on animals, peptic ulcers arise in such a large proportion of the animals thus experimented upon, that we have a right to conclude that they are directly attributable to the method pursued. When I speak of peptic gastric ulcer I mean the typical "chronische magengeschwür" as described by Hauser. For defects can be produced in the dog's stomach, for instance (and the literature on the experimental production of gastric ulcer proves this conclusively), which are not true gastric ulcers, but simply ulcerating lesions, which heal rapidly. Gustav Fütterer has produced such lesions by applying to the stomach caustics, ligating the gastric arteries, cutting off the supply of nutrition by stitching large portions of the mucosa with catgut sutures. Defects resulted, but they all healed in a short time. Even when one-third of the quantity of the animal's blood was withdrawn such defects had healed in two weeks. In 1896 Silbermann[2] produced gastric ulcers in dogs by either tying the gastric arteries or causing emboli in them by injecting suspensions of lead chromate. Thereafter he injected hæmoglobin and pyrogallic acid. When Fütterer resected the gastric mucosa, as stated before, and made injections of pyrogallic acid, he could confirm Silbermann's results, and produced ulcers of the stomach which in every histological detail corresponded to the chronic gastric ulcer of the human being. By making use of this method employed by Fütterer and Silbermann I was successful in producing experimentally gastric ulcers in one series of experiments; eleven dogs out of thirty operated upon developed typical gastric ulcer.

Now I had a method by which this characteristic lesion could be produced experimentally. The next question was, "Could these lesions be in any way experimentally transformed into adenocarcinoma of the stomach, or could they become transformed into adenocarcinoma spontaneously, as has been definitely known to occur in the human being,

[1] See Hemmeter's "Diseases of the Stomach," third edition, p. 491.

[2] Experimentelles in klinisches zur Lehre von Ulcers Ventriculi rotundum. Deutsch. med. Wochenschr., 1886, No. 29, p. 497.

and as Fütterer has observed, to occur in a rabbit, in which he had artificially produced a gastric ulcer by the method described?"[1]

Hauser has described a structural characteristic of the adenocarcinoma of the stomach, which had developed on the basis of a gastric ulcer, and which is not observed in ulcerating carcinomas not developed on this basis. This characteristic by which the so-called "ulcus-carcinomatosum" can be recognized, consists in a very peculiar behavior in the fibres of the chief muscular layers of the stomach, and also of the fibres of the muscularis mucosæ. This peculiar behavior of the muscularis consists in an oblique ascension of the fibres of the true muscular layer, and a descension of the fibres of the muscularis mucosa, the fibres of both muscular layers converging toward and fusing into each other in front of the edge of the ulcer, which is here composed mainly of connective tissue. The true muscularis bends upward in continuity, and the border of the ulcer, which is composed of very dense connective tissue, is limited by the lower or peritoneal strata of the turned-up true muscularis.

Another feature of the ulcus carcinomatosum is that a section made perpendicularly to the surface of the stomach, and through the entire bed of the ulcer, almost invariably exhibits the general outline of a fish-hook.[2] For the causes which bring about this fish-hook formation,[3] the main reason being that the lower edges of the ulcer near the pylorus are, during the efforts of gastric peristalsis to evacuate the chyme into the duodenum, exposed to the most mechanical irritation, and, accordingly, Fütterer has shown that adenocarcinoma, if it develops from an ulcer, always develops from the lower edge. This location for the development of gastric ulcer had already been emphasized in a publication by Dr. Delano Ames and myself, but it is the merit of Fütterer to have emphasized this point as an etiological factor in the causation of ulcus carcinomatosum.

I should add that in repeating the experimental production of gastric ulcer, according to the methods of Silbermann and Fütterer,[4] I not only produced mechanical defects, and injected pyrogallic acid in the method described, but I maintained a very high acidity for free HCl in the gastric chyme of the dog by supplying this acid in his food and also pouring it into his stomach through a soft rubber tube. In February, 1900, I came into the possession of a mongrel fox-terrier, who persistently vomited his food. The vomit contained no free HCl or ferments, and at the autopsy a cancer of the stomach was found near the pylorus. Transplantations with this material were made into the stomachs of other

[1] Loc. cit., p. 152.

[2] See Hemmeter, "Diseases of the Stomach," third edition, plate ix., opposite p. 506; also New York Medical Record, loc. cit.

[3] Loc. cit., p. 112.

[4] New York Medical Record, September 11, 1897.

fox-terriers, but I was not successful in producing a gastric carcinoma in any other animals inoculated.[1]

In the meanwhile the publication of Fütterer appeared, and it occurred to me that possibly my failure to successfully transplant canine carcinoma was due to the fact that the stomach of the animal into which the inoculation was made was not in a susceptible condition, and that it must be transformed into such a condition by a previous injury. This previous detriment to the tissue, in order to secure successful transplantation of the tumor, has in the case of rats not been found necessary by Leo Loeb and M. Herzog. I did not succeed in securing another dog affected with carcinoma of the stomach until after I had read Fütterer's work in 1901, and this second dog presented an adenocarcinoma which developed spontaneously at the edges of an experimental gastric ulcer. It presented the behavior of the two layers of the gastric muscularis, as first described by Hauser, had a distinct fish-hook form, and exhibited heterotopia of gastric glands, as first described by Virchow[2] and Hansemann.[3] This gastric cancer reached the size of a walnut, and two metastases were found in the omentum. It was this carcinoma which was used in making a filtrate with which the edges of the peptic ulcer previously produced in other dogs were injected.

It will be seen that these experiments are attended with unusual difficulties in procuring the material, for if we wish to study the effect of extract of adenocarcinoma upon experimentally produced gastric ulcer, we must have two sets of animals: one presenting the cause and the other the gastric ulcer. If we should accidentally come across a dog with an adenocarcinoma it would take at least two or three weeks to get a number of other dogs having experimental gastric ulcers. It is a matter of great difficulty to determine in the live animal whether it is really afflicted with gastric cancer, and if the cancer is accidentally found at autopsy in a veterinary school, it rapidly decomposes, and unless kept on ice the canine gastric cancer becomes useless for experiments in two or three days, for bacteria, especially the pus cocci, are great hinderances to successful transplantation, as Loeb[4] has emphasized. We will, therefore, in future, have to depend on cancer tissue gotten from living dogs, or soon after the autopsy, or such cancer tissue produced experimentally by the method of Fütterer, which in my experience only succeeds in one-third of the animals experimented upon.

[1] Sepsis followed a large proportion of the operations, and I could not secure the aid of a competent surgeon who would do these operations aseptically for me. A sterile extract of part of this canine carcinoma was also made and prepared for inoculation and injections into dogs, in which I expected to cause gastric ulcers. A very small quantity of filtrate (48 c.c.) was thus saved, as the largest part of the tumor had been used for transplantations.

[2] Virchow's Archiv., Bd. 111.

[3] Loc. cit., p. 195.

[4] Loc. cit.

The adenocarcinoma which developed at the edges of the experimental peptic ulcer was found at a time when I was engaged in producing such ulcers in a series of animals. Eight transplantations of such tumor particles were made into the edges of peptic ulcers of other fox-terriers. Five of these animals died of infection and other intercurrent accidental complications. Three of them lived each three months after the transplantation, and of these three, two had developed adenomatous proliferations closely resembling carcinoma at the edges of the gastric ulcer nearest the pylorus.

Summary. Eight dogs afflicted with experimental peptic ulcer, inoculated by injecting tumor particles made of suspension of the tumor cells of a gastric adenocarcinoma into the edges of the gastric ulcer. Five of these animals died of sepsis, etc., three of them lived three months each, developed symptoms of gastric carcinoma, and in two of them the adenomatous proliferations described by Hauser and Fütterer were evident at the pyloric edge.

This method of inoculation by a suspension of the tumor cells was preferred to transferring actual pieces, because I had a very small original tumor to start with, and for the purpose of demonstrating the principle involved, it makes no difference whether we transfer large pieces or only a few cells, for any ensuing development of carcinoma can only in these cases be attributed to a further growth of the injected carcinoma cells, or whatever hypothetic micro organism or tumor producing agency they may be assumed to carry. My main object, however, was to discover whether the cancer formation at the edges of gastric ulcers could be induced by the injection of a fluid gained from canine carcinoma and free from carcinoma cells as well as micro-organisms, as far as our modern methods of testing these two points permit us to judge.

Production of Efforts at Adenomatous Proliferation from the Edges of Pre-existing Experimental Gastric Ulcer by the Injection of Cell-free and Sterile Extract of Canine Gastric Adenocarcinoma. The sterile and cell-free extract of canine gastric adenocarcinoma was prepared by grinding up non-infected portions of this cancer in a sterile mortar with quartz sand, together with physiological salt solution. Then this emulsion was filtered through a Pasteur filter, and cultures made upon a number of the most commonly used media, which proved negative. In order to exclude the possible action of bacteria, I might of course have used strong antiseptics in the solution, such as bichloride of mercury, formaldehyde, carbolic acid, etc. There are, however, two grave objections to this way of proceeding. I shall have to premise what I intend to say by stating that I had from previous observations and experiments gained the impression that the tumor producing agency in these cases was not the cell itself, nor a

micro-organism, but an enzyme, which had passed through the filter. The first objection to using antiseptics or heat in sterilizing the filtrate was that whilst they no doubt could destroy any micro-organisms, a sufficient degree of heat, as well as the more effective antiseptics, would also destroy any possible enzyme present. The second objection to using these substances was that any possible effect upon transforming the peptic ulcer might have been ascribed to the antiseptic use or to chemical additions to the filtrate and not to any inherent qualities derived from the original tumor. I have, however, shown that thymol, even in saturated solution, has no such destructive action upon the proteolytic ferments of the intestinal canal.[1]

A. S. Loevenhart and Kastle, in their beautiful investigation on the reversibility of the action of lipase[2] and Loevenhart in his researches on lipogenesis[3] toluene was used to keep the tissue extracts sterile, and evidently the effectiveness of lipase was not impaired by this antiseptic. In one of my successful experiments I also made use of toluene, and I believe this excluded the possible action of any bacteria that might be presumed to pass through a Pasteur filter. From the investigations of William G. Wherry[4] concerning the permeability of the Berkefeld and the Pasteur-Chamberland filters to bacteria of small size it seems justifiable to conclude that bacteria of small size can pass through them. The bacillus producing pneumonia in guinea-pigs, for instance, will pass through the pores of a small Berkefeld filter, No. 5, and sometimes organisms which do not pass through the above filters, like the bacillus coli communis, may grow through. Referring once more to the work of Herzog, it seems justifiable to conclude from the results of Wherry, that if the virus of a disease passes through the pores of a Berkefeld filter, it is not necessarily ultramicroscopic. The practical import for our research was that we could not rely exclusively upon filtration, but had to resort to some antiseptic in order to attain an absolutely sterile liquid. For this purpose thymol, and in some cases toluene, were used.

As far as the methods at present at our disposal permit me to judge, the filtrate extract used for these inoculations was sterile. The injection of filtrate into ten animals afflicted with experimental gastric ulcer resulted in four of them in the development of adenomatous proliferation closely resembling an adenocarcinoma at the edges of the ulcer. The time in which the animals were examined after the first injection varied

[1] Hemmeter, "Ce que Deviennent les Ferments Digestifs—Bacteries proteolytique du Colon," XIII. Congres International de Médecine, Paris, 1900, also "Ueber das Vorkommen von Proteolytischen und Amylolytischen Fermenten in Inhalt des Menschlichen Kolens," Pflüger's Archiv. f. die ges. Physiologie, Bd. 81, 1900.

[2] American Chemical Journal, xxiv., 1900.

[3] American Journal Physiol., vol. vi. p. 331.

[4] Journal of Medical Research, November, 1902.

from twelve to fifteen weeks after the first injection. The histological characteristic of the carcinomas developed corresponded closely to those described by Hauser and Fütterer: (1) There was a diffuse proliferation of glands; (2) heterotopia of gland cells; (3) the cells of the proliferated gland ducts stained apparently as deeply as the normal cells in the same section; (4) there were numerous mitoses in the proliferated gland cells, some of them atypic, and also mitoses in the connective tissue cells close to the proliferated glands. Notwithstanding these histological characteristics, I am by no means of the opinion that the proliferation produced in this way was really a malignant neoplasm, for I have observed such proliferations around two peptic ulcers that were excised by operation, and the patients remained well eight and nine years respectively.

The question arises if the adenoma thus produced was not caused by the implantation of a carcinoma cell, nor by infection with bacteria, what did cause it? This question opens a wide field for reflection. If the Pasteur filter can keep bacteria as well as cells from passing through, the incentive to growth can only have been given by some chemical substance capable of passing through the filter, and contained in the filtrate. This substance was extracted from a pre-existing carcinoma in a dog. But it is essential to bear in mind that in one case the gastric ulcer developed into a carcinoma spontaneously. Evidently the cellular tissue of the stomach, in its abnormal condition, is capable of producing in itself the tumor forming agency, and whatever a tissue can produce out of its own cellular structure, if it can be proven that the tumor producing agency is not a bacterium, must be a product of the cells themselves, and very probably inherent in the cells.

Comparisons of the Relative Osmotic Pressures of Normal Cells and Carcinoma Cells of the Same Organ. Normal cells, as well as carcinoma cells, can be isolated from their stroma by pencilling portions of fresh tissue in salt solution, isotonic with the blood plasma. The strength of this solution will vary with different animals. The serum of human beings is, according to H. J. Hamburger,[1] isotonic with a 0.84 to 0.89 per cent. solution of sodium chloride. I have observed cells from a carcinoma of the stomach in such salt solution on the warm stage, and compared them with the cells of normal stomach tissue. Whilst there was no apparent change in the normal gastric cells the gastric carcinoma began to contract in the course of the day, four to five hours, as if they were in an hyperisotonic solution. Not all cells of gastric carcinoma that are pencilled out in an isotonic salt solution will show this contraction. One notices that in perhaps one-fourth to one-

[1] Osmotischer Druck und Ionenlehre, p. 445.

third of the cells there is no contraction evident. I have gained the impression that although carcinoma cells represent cells that are emancipated from the laws of normal proliferation (if I may speak of such laws), nevertheless the carcinoma cells themselves, although alienated from the general cell state, may be healthy or diseased. By healthy in this sense I do not mean that they are normal cells; but simply that they represent a condition of the cells as occurs in the majority of cancers before they begin to disintegrate. When a cancerous tumor undergoes necrobiosis certain of its cells undergo a still further pathological process and it is in these cancers undergoing cellular destruction in which the perfect lawlessness of the cancer cell becomes manifest. I am of the opinion that those cancer cells which do not act like the majority in isotonic salt solution are perhaps already undergoing the beginning changes of necrobiosis. The majority of cancer cells show a contraction, whereas this minority does not show this phenomenon. Difference in staining of the protoplasm and chromosomes can also be observed in these two kinds of cancer cells. I am in doubt whether this phenomenon of contraction or swelling, as the case may be, would be possible in the cells of all types of cancer. The adenocarcinoma of the stomach is derived from an epithelial and glandular cell which even normally gives evidence of marked regenerative power. It possesses marked mutability, as Virchow would say, and these powers are still manifest when this cell becomes emancipated from the normal laws of proliferation. I have not been able to try the experiment, but I doubt whether the cells of an osteoma, chondroma, or scirrhus would be capable of undergoing visible osmotic changes under the microscope, no matter how different the osmotic tension of their environments would be made from the tension existing within their protoplasm.

Similar observations were made with the cells of a mammary carcinoma, comparing their behavior to that observed on normal mammary gland cells in isotonic solution. I have also compared the behavior of normal gastric gland cells with those of a gastric adenocarcinoma after they had been pencilled out in the blood plasma of the same patient, and also in the blood plasma of another but normal individual. The same differences were found between the two in blood plasma as observed in isotonic salt solution. These studies led me to suspect that a deep-seated disturbance exists between the osmotic tension of the living cells of a cancer and the surrounding juices, mainly because the cancer cells act differently from the normal cells of the same tissue when placed in the same isotonic solution or in blood plasma of the same individual. Thus far these studies have been made only in mammary and gastric adenocarcinoma, and I would caution against the extension of the observations to all forms of tumors until these have been thoroughly studied in this way. It must be emphasized here that as

these pieces of tissue could only be gained at operation, I was restricted in my search for normal cells to tissue in the immediate neighborhood of the malignant growth. It is probable that cells of the same organ, more remote from the malignant growth, might have shown a still greater contrast. I am now studying the behavior of normal cells observed in cancer juice expressed from a cancer of the same organ. Normal cells of an organ observed in such cancer juice will give evidence of swelling in the course of three to five hours. These phenomena might be interpreted by differences in osmotic tension between the protoplasm of the cell and the surrounding solution. For instance, if a normal cell swells up in filtered cancer juice, we may be correct in assuming that it takes up water, that the cancer juice contains relatively more water than the protoplasm of the cell. Increase of volume of the cell, if associated with cytolysis, may be due, however, to the presence of toxic substance in the cancer juice. This has at present not yet been satisfactorily investigated. The fact that the majority of healthy cancer cells contract in salt solution isotonic with blood plasma would indicate that they have lost water. It is justifiable to assume that the osmotic tension between a cancer cell and the normal cancer juice as existing in its environment is isotonic, for a cancer cell will not change its volume in cancer juice. However, in the production of this juice it is unavoidable that the cancer cells are cut and bruised and considerable of the cytoplasm of the cancer cell may be contained in it, which is not present in the juice bathing the cancer cells in the ordinary state of these growths. Material is very difficult to obtain, for although the cancer tissue is readily obtained from operators, they do not, as a rule, cut far away from the limit of the growth into the normal tissue in an effort to remove it.

These are purely physical conditions, but they show a definite disturbance of osmotic tension.

Phenomena of cell division are as Bütschli, Quincke, and Jacques Loeb believe, phenomena of protoplasmic streaming. They require, as Quincke has shown, a definite degree of viscosity. We have to remember that all life phenomena, normal as well as abnormal, are ultimately due to motion, or changes occurring in colloidal matter.[1] No protoplasmic motion can occur if the normal viscosity of this matter is disturbed in either direction, that is, if it is too great or too small. It may be that the disturbances in osmotic pressure, which I have suggested in the preceding, may lead to changes in the viscosity of cell protoplasm, either favoring or inhibiting cell division.

Changes in Volume Which Normal Cells Undergo in Cancer Juice. Studies on osmotic pressure made by means of the hematokrit,

[1] Jacques Loeb, "The Comparative Physiology of the Brain, etc., p. 14.

according to the methods of Hedin[1] and Köppe,[2] indicate that normal cells of the stomach or mammary gland cells when placed in cancer juice derived from a gastric or mammary cancer, swell up as if they were in a hypisotonic solution. The red blood cells of normal human beings and also of cancer patients will lose some of their coloring matter when placed in sterile cancer juice or sterile filtrate made as described in the preceding portion of this article. This would, in some of my studies, occur even when this filtrate or cancer juice was made isotonic with the blood plasma, and is suggestive of a substance in the cancer juice which is capable of making the stroma of the blood corpuscles permeable to toxic or other substances capable of effecting dissolution of the hæmaglobin; and reminds one of the experiments of Belfante and Carbon,[3] and also those of J. Bordet.[4] These experiments demonstrated that toxic substances are formed in the blood serum of animals into whom blood of another animal species had been injected. If the blood of a rabbit is injected into the peritoneal cavity of a guinea-pig, the serum of the guinea-pig blood will acquire the property of destroying the red blood corpuscles of rabbits, a property which the serum of normal guinea-pigs does not possess. If 5 c.c. of serum of a normal guinea-pig are injected into the circulation of a rabbit, this animal is in no way influenced thereby. But if this serum is derived from a guinea-pig which has previously received several injections of rabbit blood, then it becomes dangerous to a rabbit. A few minutes after the injection the rabbit dies and the autopsy reveals extensive dissolution of the blood and numerous hemorrhages as a consequence. Similarly the blood of the guinea-pig can be made to acquire a destructive property upon cholera bacteria after a small amount of a culture of cholera vibrios have been injected into the peritoneal cavity of the guinea-pig. Ehrlich and Morgenroth[5] and the other authors agree that this hæmolytic and bacteriolytic action of guinea-pig serum is due to two substances, one of which they speak of as a "sensibilisator," and the other as an "alexin." It is the penetration of the "alexin" into the red blood corpuscles which makes it lose its coloring matter, but this "alexin" cannot work unless the blood corpuscles have been sensibilized by the other agent. The "sensibilisator" is formed in the circulation of the guinea-pig by the intraperitoneal injection of rabbit blood. The "alexins" are normally present in the circulation of the animal. It was discovered that the sensibilizing substance can tolerate a temperature of 70° C. without destruction, but that the "alexin" is destroyed at a tempera-

[1] Skandinavisches Archiv. f. Physiologie, 2, 134, u. 360.
[2] Dubois-Raymond's Archiv., Physiol. Abt., 1894, 154.
[3] Referred to by Metschnikoff, Annals of the Institut Pasteur, June, 1900, No. 6, p. 370.
[4] Ibid., October, 1898, April, 1899.
[5] Berliner klin. Wochenschr, 1899, Nos. 1 and 22.

ture of only 55°. I have said that the normal serum of the guinea-pig contains "alexins," which are preserved, of course, in the serum made active against the blood corpuscles of the rabbit. If the active guinea-pig serum is heated to 55° the "alexin" is destroyed, but the sensibilizing substance remains active. In such a serum the rabbit blood corpuscles retain their coloring matter, for the "sensibilisator" is not capable of producing hæmolysis. But as soon as serum from a normal guinea-pig or a normal rabbit is added, the coloring matter of the blood corpuscles begins to part from the red blood cells, for both the normal guinea-pig as well as rabbit serum contain "alexin." These agents which produce hæmolysis partake of the nature of catalytic agents. Ehrlich and Morgenroth speak of "*Zwischenkörper*" (intermediate bodies), and also of "*complement.*" In none of these investigations is it stated that these substances have been isolated.[1] The speculations concerning them are based exclusively upon an observation of their effects. They were important for me, however, in suggesting the idea that perhaps the cell growth representing cancer might in some way be associated with the influence of a catalytic agent which could be studied in a similar manner by its effects on the normal cells of the same tissue or upon the blood cells of the same or normal individuals. The effects which I have observed of cancer juice on normal cells of the same organ, and of cancer juice and cancer filtrate upon blood corpuscles, throw no direct light upon the pathogenesis of malignant growths. They were undertaken merely because such studies had, to my knowledge, not been undertaken heretofore, and I felt that I was following the injunctions of Julius Robert Mayer that a phenomenon should be studied from every possible aspect before we should seek consolation in an hypothesis. Then again there was the hope that some reaction might be discovered whereby we might be enabled to tell what was a malignant growth and what was not, by the effects of the juices of a malignant growth upon normal cells. This has, so far as my work is concerned, not as yet been successful. The question is so manifold and the liability to error in whatever direction one goes is so great, that no practical conclusions should as yet be drawn. A weak point of these investigations consists in the fact that the juices and filtrate extracts of benign growths have not as yet been studied in their possible action upon cells of the same organ, or upon blood cells, nor even have the tissues and filtrate extract of normal tissues in their actions upon each other been studied satisfactorily. The question might be asked, "Does the tissue of an entirely normal stomach contain an agent concerned in the cell growth of gastric tissue which on being extracted from a whole stomach, concentrated by aseptic evaporation, and injected into normal

[1] I shall apply the inspiration gained from the work of Bordet, Ehrlich, etc., in the explanation of the rarity of metastases, under the heading of "Metastases," later on.

gastric tissue of another animal of the same species, will cause increased growth of that tissue?" For the development of the growth of the mucosa we would have to limit ourselves entirely to extracts of the mucous membrane, for the stomach contains layers of widely different cellular structure. If such an extract of mucosa does not affect the normal stomach would it cause cell proliferation after being injected into the edges of a gastric ulcer? As the difficulties of this investigation seem almost insurmountable, depending largely on procuring proper and abundant material, I have given expression to these suggestions with the hope that they may be of value to other investigators.

This much I will have to emphasize, "Whatever the substance or agent may be which causes a benign canine gastric ulcer to be transformed into an adenoma," it is destroyed when the filtrate is heated to 60° C. (140° F.); for while four animals out of ten injected with the unheated filtrate developed adenoma, no such result followed in six animals afflicted with gastric ulcers when they were injected with the filtrate that had been heated to 60° C.[1]

Problems of Cell Growth. All of these questions are intimately related with the *problems of cell growth.* The immediate and specific causes of cell division are still imperfectly known. Is cell proliferation due, as Ribbert[2] thinks, exclusively to the removal of inhibition or restrictions to growth in the environment of the cell, or is it due to proliferative forces within the cell? We have thus two conceptions of the immediate causes of cell growth, one without and the other within the cell. According to Thiersch and Boll, each tissue continues to grow up to the limit afforded by the resistance of neighboring tissues or organs. In the fully developed body the mutual relations of the cells are of such a nature that the conditions for further proliferation are unfavorable. Ribbert and others express this in the term "tissue tension" (*"Gewebe spannung"*), which prevents an increase of growth in the cells. They understand by this "tissue tension" all the mutual influences of the tissue constituents upon each other; they do not exactly mean mechanical pressure, although this no doubt plays an important rôle in restricting growth. The removal or lessening of this resistance to growth through injury or disease causes the resumption of growth and cell division, leading either to regeneration of lost parts or the formation of abnormal growth. According to the precedent of Virchow, it was formerly held that not only the function of a cell, but also its growth could be directly caused by the action of external stimuli. Virchow distinguished, accordingly, between functional, nutritive, and formative stimulation. This doctrine

[1] I am refraining from designating the proliferation as carcinoma for reasons given at end of article.

[2] Loc. cit., p. 300.

was contested by Weigert, whose efforts to disprove the power of external agencies to stimulate directly cells to proliferation have been very instructive. Weigert postulates that some primary injury to the tissues, as the immediate effect of chemical, mechanical, and other external agencies, is necessary to stimulate growth. This postulate has been fulfilled in many instances where such a cell injury had not been previously suspected. Better methods of investigation will no doubt enable us to demonstrate such an injury to the tissues. At the same time it is going too far, in my opinion, to attribute all morbid cell growth to such cell injury. In a comprehensive way Weigert's theory may be stated as follows: Cells are incited to growth through removal of obstacles to growth in the environment, in consequence of some disturbance in the normal relations or equilibrium of the cells with surrounding parts. The capacity of cells to proliferate has become latent when a certain "tissue tension" has been reached; it has become potential by the establishment of definite relations between cells themselves and between the cells and the basement substances, bloodvessels, lymphatics, tissue juices, and chemical substances contained in them.

We have hitherto studied cell growth as conceived to be due to a removal of restriction to proliferation outside of the cell body. In all these cases, however, it is difficult to determine the immediate stimulus to cell division, for a long chain of causes and effects may intervene between the primary disturbance and the ultimate reaction of the dividing cells. The opinion is gaining ground that the immediate causes of cell proliferation, whatever their antecedents, are to be sought in local chemical changes. Recent experiments on the proliferation in the ova of various invertebrates, conducted by Jacques Loeb, T. H. Morgan, R. Hertwig, and Mead, give ground for the conclusion that the stimulus to cell growth is of a chemical nature.[1] The climax of these experiments is reached in Loeb's artificial production of parthenogenesis in sea-urchin eggs by treatment with dilute magnesium chloride. The remarkable gall formation in plants leaves no doubt that extremely complex abnormal growths may result from specific chemical stimuli, and pathologists have held that abnormal growth in the animal body may also be incited by abnormal local chemical conditions. Only in two ways, then, can the cell be incited to growth—either by the removal of resistance to growth in the environment or by an increase in the formative energy resident within the cell. William H. Welch[2] concedes both of these possibilities—*i. e.*, forms of energy acting from without directly increasing the formative energy of the cell, and stimulating it to growth and multiplication; and, secondly, increase of the proliferative forces natur-

[1] Edmond B. Wilson, "The Cell in Development and Inheritance," second edition, p. 391.

[2] Adaptation in Pathological Processes, THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, June, 1897.

ally latent (dormant) within the cell. It will be difficult to decide in which of the two ways cell proliferation is brought about. One reason for assuming that in carcinoma of the stomach the tumor producing agency is to be sought in increase of the proliferative forces within the cell is the fact that these cells must be ground up and crushed very thoroughly before the extract will have any cancer converting effect upon experimental gastric ulcer. If the tumor producing agency were some chemical substance in the environment of the cell, we should not expect that thorough crushing and grinding were necessary to extract it, but that it could be dissolved out by repeated percolation and irrigation. However, this is an unreliable test, as the tissues must be torn up into small pieces in both instances, even if only to permit percolation. The fact that it is possible to extract a tumor producing agency from gastric carcinoma by crushing pieces of it in normal salt solution would not permit us to decide whether the tumor producing substance was derived from within or without the cell.

The modern view that cancer metastases can be effected by the transportation of single carcinoma cells is a support of the contention that the tumor producing agency is resident within the structure of the cell. In a recent investigation on the fate of dislodged and embolized tissue particles in the animal body, Paul Lengermann comes to the conclusion that the power of producing metastases is dependent upon an increase in the proliferative energies inherent in the cell, and not upon a reduction of normal tissue resistance to growth.[1]

Speaking of the influence of cell nutrition and the maintenance and undisturbed progress of cell function, Ludolf Krehl[2] says: "Nobody will expect that a tissue can maintain form and size without sufficient supply of potential energy; but the incentive does not come from the blood, as was formerly believed, but always from the parenchyma itself."[3]

Influence of Physical Laws on Cell Growth. Oscar Hertwig investigated the influence of temperature on the recently fertilized ova of rana fusca and rana esculenta, and found that certain well-recognizable stages ("Stadien") in the development of these eggs were reached quicker as the temperature of the breeding medium was increased.[4] He found that the same relation existed between rate of growth and temperature as was known to exist between reaction time and temperature.

Cell volume, within certain limits, is dependent upon osmotic pressure.

[1] "Schicksale verlagerter u. embolisierter Gewebsteile im thierischen Körper," p. 69, in "Arbeiten a. d. Pathol.-Anat. Abtheilung d. kgl. Hyg. Institut." Posen, 1901, s. 299, O. Lubarsch.

[2] Patholog. Physiologie, second edition, p. 532.

[3] "Nicht von aussen zugeführte Kräfte bringen das Heil, sondern die Zelleschaft es sich selbst."

[4] Archiv. f. mik. Anat. u. Entwicklungsgesch, 1898, 52, 319.

Cells can be made to undergo apparent growth by placing them in solutions the osmotic pressure of which is below the pressure within the cell protoplasm. In this case the cell volume increases by the diffusion of water into the protoplasm. Loeb[1] cut off the polypi from colonies of tubularia, and brought the stems in sea water of various concentrations and dilutions. He found that polypi again grew out of the stumps as long as the sea water was not concentrated to more than 70 per cent. of its volume or not diluted more than to 225 per cent. of its original volume with water; but the regeneration occurred prompter and quicker in the diluted than in the concentrated sea water. Loeb's experiments show conclusively that moderate dilution of the external medium in which a cell is bathed favors growth—*i. e.*, the solution outside must be a hypotonic one. Two other essential physical conditions to growth are (1) a certain turgescence (turgor) within the cell, and (2) expansibility of the enclosing protoplasmic envelope.

It is conceivable that cell protoplasm will become more expansible and looser by the reception of water from the hypotonic environment and a certain turgescence—that is, a hypertonic state within the cell metabolism, and the consequent increase of osmotic energy connected therewith. Increase of turgidity is always seen in rapidly growing parts. Turgidity means osmotic entrance of water into the growing cell. Claude Bernard[2] found that blood flowing through a secreting gland had lost water, and Ranke found that blood that had streamed through a working muscle had lost water.[3] To complete the logic of these instructive observations, Loeb demonstrated that the water thus lost was taken up into the substance of the working muscle; for when the muscle while at rest and before work was placed in a solution which was isotonic with the protoplasmic contents of the muscle cell, it increased in weight during its work[4]—that is, the augmentation of metabolism during work had evidently increased the osmotic pressure within the muscle cell, and the ensuing difference in pressure had induced the growth.

These observations are important for the interpretation of my own studies demonstrating the contraction of fresh cancer cells in solutions made isotonic with the human plasma, or in blood plasma itself, as if they were in a hypertonic solution—a phenomenon not observed when normal cells of the same tissue from which the cancer was taken are placed in the identical plasma or solution. It will hardly be necessary for me to emphasize that any and every growth of and in cancer cells cannot be attributed to the taking in of water only, nor can a muscle hypertrophy due to work be attributed to the taking in of water exclu-

[1] Organbildung und Wachstum, Würzburg, 1892.
[2] Phénomènes de la vie, 2d edit., i., 169.
[3] Tetanus Physiologie, 1868, 89.
[4] Pflüger's Archiv., Bd. lxxi., 439.

sively. The water osmosis is only one phase of the process of growth, that phase which by effecting an increase of volume impresses us most as growth. The internal construction of the cell household, the deposition of new cytoplasm, is concealed from us.

When frog larvæ are analyzed at different stages of development for their percentage content of water and solid substance it is found that the entire growth of the first fourteen days consists in the incorporation of water. The body weight becomes ten times as great by water, and not until after this does the interior construction and the deposit of solid substances into the aqueous tissue begin. In the first two weeks of development of batrachian larvæ the percentage of water in the embryo rises from 56 per cent. to 96 per cent.,[1] thereafter it begins to sink again. In the light of our present knowledge we have a right to speak of the "osmotic pressure of the cell," for the cell protoplasm, as previously emphasized, is a liquid, a solution, or at least in a state of viscosity. The entrance of water into the cell substance is brought about primarily by metabolic changes effecting a hyperisotonic state in the cell with regard to its surrounding liquid environment. *This phenomenon of change of dimensions (contraction) of fresh carcinoma cells (gastric adenocarcinoma in normal plasma or solutions isotonic with plasma) is to me strong evidence in favor of the view that whatever other causes for the excessive growth of malignant cells there may be, certainly some of the causes are resident within the cell protoplasm itself.*

When we approach a consideration of the question of how the cell builds up protoplasm—that is, an inquiry into the methods and means by which it carries on the synthesis of its substance—we are confronted with a problem apparently presenting insurmountable difficulties, for all artificial syntheses are brought about by forces and agents which can never be conceived as participating in the processes of life. Such agents and forces are high pressure and temperature, concentrated inorganic acids, free chlorine, and galvanic currents of high tension. All of these are factors which would destroy cell life instantly.

So far we know definitely of the synthesis of albumin is only by the aid of enzymes (catalysator). For instance, the reconversion of albumoses, which have been formed in the gastro-intestinal canal into albumin, is attributed to some agent in the gastric wall.[2] When the stomach is isolated from an animal, but kept alive, at the height of digestion all albumoses disappear from it. It might be presumed that this does not indicate a synthesis, but a further breaking down of the albumoses. In that case, however, an increase in the non-precipitable nitrogenous substance should be demonstrable, which is not the case;[3]

[1] Davenport. "Rôle of Water in Growth," Proceedings of the Boston Society, 28, 73, 1897.
[2] Hofmeister. Zeitschr. f. Physiol. Chemie, 6, 69.
[3] Glässner. Beitr. z. Physiol. u. Pathol. Chemie, 1902, i., 328.

so that any other interpretation of this disappearance of albumoses, except their synthetic reconversion into albumin, appears illogical. Furthermore, Danilewsky and Sawgaloff have proven that chymosin (rennin) is capable of synthetically constructing an albumin from peptones and albumoses in an acid medium. This albuminous body, which they designated as "plastein," is soluble in weak acids and alkalies, insoluble in water, and can be precipitated by strong salt solution—undeniably a typical albumin constructed synthetically by this ferment.

It would be going too far to assume that all syntheses in the organism are enzyme syntheses, for an enzyme (catalyzer) is *incapable of producing anything that would not also be produced without it by other means.* Ostwald[1] groups all ferment or enzyme actions under the term "catalyse," by which he means the *acceleration of a slow or the retardation of a rapid chemical process through the presence of a foreign body (catalysator).*[2]

This definition gives the specific characteristic of enzyme action. An enzyme can, therefore, not carry out a process which would be impossible without it, but it can only influence the time in which a chemical process occurs, generally increasing the rate of the reaction, which would also take place, in a much slower or faster manner as the case may be, however, without it.

The facts, namely (1) that albumin can be constructed synthetically by enzymes, and (2) that enzymes act merely as accelerators or inhibitors of processes that can occur without them, coupled with the experimental results briefly narrated in the preceding (acceleration of cell proliferation by injection of a cell-free and sterile fluid), should suggest the possibility that abnormally rapid formation of protoplasm such as is observed *in the marvellous cell-proliferation of malignant tumors may in some way be associated with the action of an enzyme.* The catalytic origin of malignant neoplasms is by no means proven by these facts and considerations, but only made more probable. I have previously emphasized the important rôle which physical processes (osmosis) play in the growth of cells, so that it is not logical to attribute proliferation to enzyme action alone; but as we have seen that even this osmosis is due in part to a preceding hyperisotonic state within the cell brought about by increased metabolism, the function of a catalyzer is even here not inconceivable, but on the contrary very probable. Much remains to be proven before we are justified in making this conclusion indisputable.

Thus far attempts to isolate enzymes have failed, for what are believed to be ferments are variously considered, albuminous or proteid bodies — albumoses or peptones (Uróblewski) — or nucleoproteids

[1] Loc. cit. See W. Ostwald, Ueber Katalyse, Leipzig, 1902.

(Pekelharing's conception of pepsin), in connection with which ferment actions have been observed. In brief, nothing is definitely known of the chemical nature of organic enzymes.

When it comes to the problem of isolating enzymes from protoplasm of cells we find that it presents insurmountable difficulties. It might be thought that inasmuch as enzymes are chemical substances, some of which are known to exert their characteristic action apart from the living substances to which they are usually attached, it might be possible to destroy the cell alone and extract the enzyme; but all protoplasmic poisons are also enzyme poisons (corrosive sublimate, carbon monoxide, sulphuretted hydrogen, hydrocyanic acid, nitrate of silver, formaldehyde, hydrogen peroxide). J. R. Green has emphasized that protoplasm itself has powerful fermentative activity. No matter what the exact relation is that the intracellular enzyme has to the protoplasm, whether it be conceived to be a detached protoplasm molecule or not, as long as it is considered a derivative of protoplasm it must be self-evident that protoplasm is capable of doing all those things which the enzymes can do. Newer conceptions concerning this subject attribute to protoplasm much more wonderful achievements than to the enzymes themselves. If the efforts to separate growth stimulating enzymes from cell protoplasm are at present futile, from the insurmountable chemical difficulties involved, we should realize that protoplasm itself may exert a more intense catalytic action than any enzyme derived from it. Our reflections concerning the nature of a substance which we assume to be capable of stimulating cell growth, and which is cell free and sterile, must end here for the present. We can only say that the agency is contained within the cell, but whether it be a special derivative of the cell protoplasm or the protoplasm itself, it is, in the light of our present knowledge, impossible to decide. A slight hope of advance lies in researches showing differences in the degree of temperature which the protoplasm and the ferment can stand without destruction. I have gained the impression that some ferments are much more susceptible to high temperatures than the protoplasms from which they are derived. For instance, the gastric mucosa of a dog can be heated to a temperature of 158° F. (70° C.) without absolutely destroying the tissue; but heating pepsin to this temperature for three hours will destroy its activity permanently. Similarly, when the so-called "commercial" pepsin is heated to a temperature of 55° to 60° C. in a moist condition it is destroyed (in a thoroughly dry state it may tolerate 160° for a short time). Nevertheless the chemical composition of the nucleo-albumin is still there as it was before the heating. The fermentative power has disappeared. Evidently ferments are not nucleo-albumins in the ordinary sense of the chemist, but something attached and associated with these nucleo-albumins.

Concerning the Structure of Protoplasm and its Chemical Organization. The method that has become most common to familiarize us with the structure of living substance has been to start from histological elements visible under the microscope and to attribute certain physiological functions to them. The conceptions thus derived have not always acquired precision, and we have definite notions only concerning the coarser elements visible under the microscope, such as the nucleus, the chromosomes, etc. This method of observation has not been able to give the least explanation of the finer elements of the cells, the innumerable droplets, barely visible vacuoles and granules of the protoplasm, not to speak of that still finer subdivision of cell protoplasm which might be designated as ultra-microscopic. It is very gratifying, therefore, that biochemists have approached the subject of the construction of the living substance from the purely chemical standpoint, as, for instance, Franz Hofmeister has done (Chemische Organization der Zelle), who did not start from the visible architecture of the cell or protoplasm, but from its achievements and functions. He tried to investigate how protoplasm must be constructed in order to make these functions possible. As the functions of protoplasm are above all things chemical, he entered exclusively upon chemical considerations.

The hepatic cell furnishes us with an instructive example of how many chemical processes may go on in one and the same cell, and very probably go on simultaneously. We know definitely that the liver cell forms glycogen from sugar, and, reversely, sugar from glycogen. It forms urea from ammonia and amido acids. It decomposes hæmoglobin, and under the splitting off of iron it converts it into bilirubin. It can manufacture cholic acid from a substance still unknown, and pairs it with taurin and glycocoll. This same cell can combine phenols with sulphuric acid to form the ethereal sulphates, and it can retain or render harmless poisons that are conducted to it. Nothing is more certain than that these performances represent only a fraction of the chemical versatility of the hepatic cell, for we must certainly assume that the same cell can in addition execute other chemical processes necessary for the oxidation of the food materials brought to it for hydration and assimilation. The supposition that there is a division of labor among the liver cells, one group of cells manufacturing one product and the other another, is untenable because the hepatic cells are of the identical structure throughout the liver, and their relation to the blood, lymph, and biliary vessels so alike that an assumption of a division of labor is not justifiable. There is no escape from the conclusion that all liver cells are chemically equivalent, and each cell is capable of performing all of the described chemical processes and possibly many more. When we reflect that all this chemical activity is invisible by the microscope,

and that many chemical processes must occur side by side simultaneously, it is difficult to conceive of the construction of protoplasm that would make such a manifold and wonderful chemical activity possible.

Many years ago Hoppe-Seyler expressed the opinion that such activities in living cells as were intelligible at his period were due to enzymes, and since then it has been possible in many cases to extract such intracellular ferments from the innermost structure of the cells and to establish their significance for vital processes. When we compare the instrumentarium—chemical substances and reagents necessary for chemical transformations in the laboratory—with the processes as they occur in living protoplasm (as much as has thus far been accurately observed) we cannot fail to be impressed with the astounding simplicity and conformity to the end in view exhibited in the means which protoplasm employs to accomplish its chemical purposes. In order to induce a reaction in the laboratory we need a reagent, *i. e.*, either an alkali or an acid, or perhaps the application of heat; but the reagents which the cell employs are calculated to fill the chemist with envy.

The food substances and the oxygen and other possible stuffs which act upon each other within the cell do not, as a rule, belong to the normal cell household, but enter it from the blood. The reagents, however, which induce the reactions, must always be present, and they must in some way be protected from being washed out of their domicile by the constant flow of liquid passing through the cell. These reagents must be either soluble in water or infinitesimally divided in it. They must be capable of accomplishing relatively large chemical performances, and not be consumed or used up during their activity. Such qualities are only known to be possessed by agents which the chemist has designated as *catalyzers*. The bearers of the chemical energy in the cell are catalyzers of a colloidal consistency (Hofmeister). According to Hofmeister, we are justified in assuming that the living cell protoplasm contains all the ferments necessary to the execution of the chemical performances observed in connection with that cell. This view is supported by the knowledge obtained of the physiological chemistry of quite a number of cells in the animal body. For instance, we know that the hepatic cell can yield up (1) a proteolytic ferment, (2) a ferment that can transform combined nitrogen of amido acid into ammonia, (3) a fibrin ferment, (4) a glykase, (5) a maltase, (6) a ferment capable of splitting up nucleins, (7) a lactase, (8) an aldehydase, (9) a lipase, and (10) a ferment similar to the gastric chymosin. Here we have definitely established the presence of ten different ferments in a single hepatic cell. *In addition to this we may believe that the synthetic construction of the cell tissue itself requires a special ferment to make possible the chemical processes necessary for the upbuilding of protoplasm.* From what I have said in connection with normal and abnormal cell

growth *it is evident that it is this ferment to which must be ascribed the power of accelerating or inhibiting cell growth.* If we once accept ten different ferments which really have already been definitely established as existing in the same cell, there is no logical reason why the remaining unexplained chemical functions of the cell should not also be ascribed to peculiar ferments, and *I can conceive of no reason why cell growth itself should not be accelerated or inhibited, as the case may be, by a particular enzyme.*

A considerable number of capable modern physiologists have accepted the view that every chemical reaction in the cell has its particular catalyzer corresponding to it. It is easy to recognize that this view may lead us too far, for the specific nature of the ferments is not always such as to restrict their action on one single chemical body, but they may be able to transform a greater or lesser number of substances of similar construction (tyrosinase, for example, may oxidize a large number of aromatic substances). Furthermore, it is conceivable that very labile bodies may arise as a result of chemical transformations in the cells, which are promptly changed into other forms under the existing conditions, and, therefore, no ferment is necessary to explain such transformation. A further revelation which modern chemistry has brought particularly through the researches of Kastle and Loevenhart, to which I have already referred, is the reversibility of the action of ferments. Should this power of reversibility of enzyme action be confirmed with other ferments, it opens up the possibility that many analyses and syntheses are brought about by the same ferment according to the existing requirements and chemical conditions in the cell.

It is probable that the chemical organization of the cell is capable of reckoning with all possibilities, whether they occur within or without the cell, whether they are an advantage or hostile to the cell state. There are no reliable reasons for believing that the organic antitoxins, coagulins, and antihæmolysins owe their origin to definite catalytic cell agents which are equipped for the production of such protective substances. M. Jacoby holds that the antibodies do not act like ferments. The cell is even equipped with ferments for the purpose of committing suicide or digesting itself when it has arrived at a state or condition in which it is no longer of use to the cell state. This phenomenon of cellular autodigestion has recently been observed in tissues which have been perfectly protected from the invasion of microorganisms.

Cellular autodigestion has been studied in all animal organs and occurs in all except those that show a very slight degree of metabolism. M. Jacoby gives to this phenomenon the designation autolysis. It is well known that the various forms of lymphoid cells contain an abundance of a trypsinoid ferment, and it is possible that autodigestion

occurs by virtue of such an enzyme. Petrey[1] found that in neoplasms autolysis was much more intense than in normal corresponding tissue. The proteid substances and the nucleins of the cell, the glycogen and the fat, are split up similarly as they would be in the intestines, and a number of diffusible substances result, such as sugar, leucin, tyrosin, fatty acids, etc. This is a form of catalytic colliquidation occurring in single cells, or in cell complexes which have passed the stage of their usefulness; and if this process occurs in an otherwise normal organism there is no reason why the end-products of such cellular autodigestion should not be taken up by the blood and lymph and be absorbed and assimilated to the advantage of the general organism just as they would be if they had been absorbed from the digestive tract.

An astounding fact which has been revealed by modern investigation in connection with this phenomenon is that bactericidal substances are set free during autolysis. It is well known that proteolytic digesting mixtures are first-class culture media for bacteria. For this reason the production of bactericidal substances during cellular autodigestion demands admiration.

If I have in the preceding suggested the probability of the action of intracellular catalytic agents in accelerating or inhibiting cell growth, I do not wish to be understood as meaning that these agents are the only factors which determine the growth and the character of the cell protoplasm. What I have said concerning the rôle of osmosis will prevent my being misunderstood in this connection. An intracellular enzyme cannot construct protoplasm out of itself—it can only build it up out of the materials furnished to it; and as these materials must vary with every species and even with every individual, it is probable that the elements of which protoplasm is constructed within the cell must be presented in a certain definite form, in order that a normal cell protoblast shall result. This is an important point, for it explains how variations in the chemical composition of the cell juices (dyscrasias) may be determining factors for the character of the resulting cell structure.

The simultaneous action of so many intracellular ferments within the same cell sometimes representing diagonally opposite processes, such as oxidation and reduction, hydration and the withdrawal of water, is only conceivable if we accept, with Professor Edmund B. Wilson, the foam structure of protoplasm, that is the view which assumes that protoplasm is held within a foam-like structure of countless ultra-microscopic compartments, retorts, or vacuoles. We must assume also that the walls of these ultra-microscopic spaces are not affected by the reaction which takes place within them. For instance, that the walls of the

[1] Hofmeister's Beitr. z. chem. Phys. u. Path., 1902, ii.

compartment or vacuole in which oxidation takes place are resistant to the oxidase, and that the walls of the space in which proteolysis takes place are resistant to the proteolytic enzyme. Such a possibility is, so far as our present knowledge goes, only conceivable within the living cell by means of its catalytic agents, which may decompose an albuminoid body of one composition completely and yet leave another very similar albuminoid body entirely intact. For instance, the proteolytic ferment of the liver can completely decompose the globulin of the hepatic substance, but it does not attack another albuminous body of similar composition with which it may even be in contact. The intactness of this so-called foam structure of protoplasm is, therefore, an essential condition for the normal action of the intracellular enzyme. A destruction of these ultra-microscopic partitions may lead to serious consequences, and it is here that the importance of what Welch calls the "more subtle and partial damage of cytoplasm and nucleus" exercises its detrimental influence in destroying the normal intracellular architecture and making possible the liberation of ferments and disturbing the normal chemical equilibrium.

We must conceive of the normal and orderly performance of the cell as brought about by the aid of an admirable and highly sensitive system, embracing among other things a transference and transformation of chemical, electrical (ions) and other specific forms of energy, and of accelerating and inhibiting enzymatic (catalytic) agents; of the latter a great variety, each acting in its own ultra-microscopic compartment. We must conceive of a delicate mutual adjustment and conformation to purpose among the many little laboratories within the cell household. And even these conceptions are coarse and inadequate if we knew in reality of the incomprehensible fineness and perfection of intracellular chemical activity. But it will be readily understood that very slight damage to cytoplasm in the sense of Welch[1] will be sufficient to destroy this beautiful arrangement, and enzymes which are useful lambs in the orderly household may become destructive lions when the partitions are broken down.

In the preceding I hope to have made possible the conception that abnormal cell growth may be due to something else than bacteria At the same time I do not wish to deny the possibility of a deleterious influence exerted by bacteria and favoring the development of malignant neoplasms. Malignant neoplasms represent a great group of abnormalities, and I agree with Hansemann that there cannot be a uniform cause for all these manifold types of abnormal cell growth. But if I admit the possibility of bacteria as active in their etiology, it is only as indirect agents in causing these more subtle and partial damages, to cyto-

[1] The American Journal of the Medical Sciences, June, 1879, p. 19.

plasm, which liberate ferments on the one hand, and destroy them on the other; for we must not lose sight of the possibility that even within the cell abnormal growth may be due to excessive action of one ferment stimulating growth, or to the absence of an enzyme necessary to inhibit it.

Reversibility of Enzymes. Basing our views on the chemical mechanism of growth on the phenomenon of the reversibility of enzymes, it is intelligible how increase in the dimensions and weight of the cell mass may be brought about by two different and divergent processes. There may be only the synthetic enzyme concerned in the control of growth, or there may be a second intracellular enzyme that inhibits growth, by analysis of protoplasm already formed. Under the conception of enzyme reversibility, however, it is not necessary to assume the existence of two distinct enzymes—one synthetic, the other analytic—for reversibility means that one and the same enzyme may exert diagonally opposite chemical effects if need be. The synthetic enzyme may act like a governor upon the metabolic machine of the cell. If the influx of utilizable substances is normal or subnormal it works synthetically and builds up protoplasm; if the influx is too great it reverses this state of affairs and breaks down protoplasm analytically. We are already very close to the view of the self-regulation of metabolism by reversible enzymes in the case of the liver glycogen, and of fat digestion and absorption. A simpler conception of glycogen metabolism cannot be held than that controlled by an enzyme which converts sugar into glycogen, when there is an excessive ingress of sugar, but reversely converts glycogen into sugar when there is an insufficient influx of sugar.

The metabolism of fat would be readily intelligible if we similarly accept the existence of an enzyme in the fat cells which would be capable by means of its reversibility of maintaining a definite equilibrium between the soaps in the blood and the fats in the fat cells, or which some enzyme (to apply the protothesis to fat digestion) were capable of splitting up fat into fatty acids and soaps within the intestinal lumen, and after their absorption recombining them into neutral fats again.

The doctrine of an intracellular enzyme being active during normal cell growth brings with it the suggestion of a detriment to this enzyme when we are confronted with abnormal cell growth. No doubt the intracellular laboratories are seriously upset, and the anarchistic growth may be due to several possible factors:

1. The self-regulating catalytic mechanism of the synthetic enzyme may be destroyed; it can only build up, no longer decompose.

2. There may have preceded a lesion to the finer structure of the cell substance, a lesion though delicate, yet irreparable, paralyzing the self-regulating catalytic metabolism.

3. The normal tissue tension in the environment of the degenerate

cell can hold it in check for a while if the lesion has struck only one or a few cells—the cell state is threatened by the leaven of rebellion, but perhaps the normal tissue equilibrium of the cell state may be restored if the anarchy has not struck too many cells; they may be forced to autodigestion, or some other form of disintegration, and for all that we know this may occur often if the cell state is vigorous and the metabolism normal.

4. But if the protoplasm apparatus of a considerable complex of cells is disturbed simultaneously, the normal cells in the environment, the tissue juices, etc., are helpless to overcome the excessive growth.

Some have argued that cancers always grow from out of themselves ("aus sicht selbst"—Ribbert); that is, one cancer cell always grows from a preceding cancer cell—until the original degenerate cell is reached. But I can conceive of no reason why the altered metabolism of large groups of malignant cells should not be able to produce such detriment, by chemically affecting adjacent normal cells, that their cytoplasm also receives a subtle damage, sufficient to paralyze the self-regulatory catalytic apparatus for growth (a kind of enzymatic, not bacterial infection). This extension of catalytic infection to other cells, even to the cells of the bloodvessels, is, of course, as yet an assumption; but it is well known that all the various tissues in an autonomous (Lubarsch) neoplasm are in a state of abnormal proliferation, particularly the bloodvessels which give evidence of a peculiar development (Klebs),[1] explainable only on the assumption that this tissue also has been drawn into the cell anarchy, but not to the same extent and character as the cells of the neoplastic parenchyma.

The cell has within its protoplasm certain recognizable structures which may be termed the organs of the cell, viz., the nucleus and its constituents, the chromatophores, centrosomes, the plastids—the passive bodies (E. B. Wilson), the metaplasm or paraplasm, the vacuoles, with their inclusions and secretions, the pigments in certain locations; all of these things signify that the cycloplasmic meshwork is not everywhere in the cell of the same chemical composition or reactive energy. This is already suggested by the fact that widely different reactions, sometimes chemically opposed to each other, occur in the same cell simultaneously. In the cytoplasm, synthetic and analytic transformations occur, not always by the same chemical reactions, but by a series of widely differing reactions. The decomposition of glycocoll to form urea, for example, is not conceivable without a liberation of the NH_2 group from a part of the glycocoll molecule, then follows an oxidation of the remainder, and eventually a combination of the fractional parts. But it is essential that these reactions should occur in well-ordered sequence, other-

[1] Pathologie, Bd. xi.

wise urea cannot be formed in this way. A lawful and ordered sequence of this and numerous similar composite reactions within the cell necessitate the conception that the different agents work separately in different compartments of the cell, we are forced to accept a chemical organization which excludes the idea that the cytoplasm is everywhere the same chemically—*in short, there cannot be an ubiquitous chemical equivalence of protoplasm.* The colloidal reagents then are separated by walls, to them impenetrable and secure from their chemical influence. Let us conceive of a lesion, invisible to the microscope but destroying these partitions, and we can realize the danger of liberation of enzymes; they can now attack all elements formerly inaccessible, or they may even attack each other.

This is the proper place to be reminded of the many theories of the causation of cancer, attributing it to some form of irritation (to which the parasitic theory may be classed also) or to trauma.[1]

METASTASES.—Virchow has expressed the opinion that malignant tumors may extend in three different manners:[2] First, by immediate propagation—that is, by direct extension or growing over from one organ into another; second, by dissemination—that is, detachment of tumor particles which settle down in another position; for instance, if a carcinoma of the stomach extends through or perforates into the peritoneum, the cells of the carcinoma may gravitate to any portion of the peritoneum and cause independent secondary growths. The third manner of extension is highly interesting from the standpoint illuminated in the preceding pages, and in order not to express the views of this great master in a wrong manner I will quote his own words: "This manner of metastatic extension makes it very probable that the transference occurs by means of liquids, and that these possess the power to create an infection ('Ansteckung'), which causes the individual parts

[1] Hemmeter. Cancer Etiology, Diseases of the Intestines, vol. i. p. 677.

It may be objected that I am here moving on very hypothetical ground, and having in the beginning of this article doubted the value of hypotheses, that I am myself now adding assumptions which go beyond the demonstrable state of facts concerning cell growth. But I must contend that I am not formulating a new hypothesis when I assume that all cell growth must be under the control of an intracellular catalyzer; I am simply for the time being using an assumption based on present observations, which, however, have not yet been sufficiently comprehensive. We know of the causal relation between cell growth, cell chemistry, and catalyzers. Certain reactions occur in the cell, certain products are built up, certain substances decomposed. We can isolate the synthetical and analytical products; we have in many instances isolated the enzymes and repeated their characteristic reactions in the test tube. We know from the nature of certain intracellular reactions that they must inevitably occur in separate compartments. Hence we are forced to believe that the growth of the cell structure itself is a separate and distinct performance, that there must be self-regulating cytoplastic syntheses in the cell, and that in pathological cell growth this chemical process is deranged. I am here making temporary use of a "protothesis" (see W. Ostwald, Naturphilosophie, s. 399), with the view that further researches may instruct us whether the assumption is correct or not. The difference between a protothesis and a "hypothesis" is that the former adds nothing to existing observations which cannot further be tested. A protothesis is a temporary conclusion drawn from experience, observation, or experiment, for the purpose of subjecting it to critical testing concerning the limit of its value and significance.

[2] Cellular Pathologie, s. 258.

to form a reproduction of the same mass which was originally present." Is it not possible that Virchow here conceived of a form of catalytic action? The other two forms of metastatic extension can, of course, not be denied. The third type, however, has been emphatically denied, and has not as yet been recognized by any pathologist of prominence.

It was Waldeyer[1] who first demonstrated by systematic investigation that carcinomas grow into the lymph spaces and vessels, and so may reach the general circulation. This observation has been abundantly confirmed; and, furthermore, the characteristic difference has been established that carcinomas readily grow into the lymph vessels, but that the bloodvessels offer them considerable resistance. (It is claimed by Hansemann that sarcomas, on the other hand, may readily break into the bloodvessels.) A number of prominent special investigators of this subject have called attention to the comparative rarity with which metastases occur by the way of the circulation, and Hansemann[2] suggests that a large part of the detached carcinoma cells are destroyed in the blood circulation.

It is essential to distinguish between the local factors which can be recognized as active in the development of a primary tumor and the general factors which determine its future fate, particularly the development of metastases. Of the local factors the most prominent ones have already been sufficiently considered, but the factors which control the formation of metastases are very manifold; and in this connection I should like to call attention to the following: (*a*) Condition of other organs; (*b*) abnormal states of the entire body, the simultaneous action or refusal to act of the regulatory apparatus of the organism; (*c*) acquired or inherited disposition, spoken of as individual disposition (the carcinoma dyscrasia). It is in this connection that the collective investigation of the German government, under the direction of Prof. E. von Leyden, gives promise of throwing light upon the cancer etiology as far as it is associated with bodily constitution, vocation, inheritance, nutrition, manner of living, etc.

In this connection I desire to call attention to a possible explanation of the rarity of metastatic extension of cancers by way of the blood circulation. The idea was suggested by the investigations of Belfante, Carbon, J. B. Bordet, Ehrlich, and Morgenroth, previously referred to. Concerning the hæmolytic action of the serum of one animal upon the erythrocytes of an animal of another species, it is necessary that the effect of the serum of normal individuals upon isolated cancer cells of other individuals should be studied, for it is conceivable that the cancer cells represent forms of protoplasm which have become *so far alienated and emancipated from the general physiological laws of the body that they*

[1] Virchow's Archiv., 1867, Bd. xli.

[2] Loc. cit., p. 91.

actually represent cells foreign to the body against which the serum brings into action its means of defence just as it would against any other foreign intruder. This is, to my mind, a very hopeful direction for investigation, with a view to prospective prophylaxis or treatment. The point of inquiry will have to be: "*Does not the organism contain in its blood serum defensive substances capable of destroying cancer cells as long as they are not flooding the circulation in excessive quantities? and, if so, how can this natural means of defence be augmented?*" The fact that carcinomas extend preferably by the way of the lymph vessels is highly suggestive of the means of defence in the blood circulation above referred to.

Critical Retrospect. In the preceding I have attempted to consider the pathogenesis of cancer from the standpoint of the chemist and physiologist rather than from the bacteriological standpoint. The principal hypotheses were referred to and the difficulties in the way of the acceptance of the parasitic theory briefly given. The changes which cells may undergo under normal and abnormal conditions were presented in the paragraph on "metaplasia." In order to narrow down the point of inquiry the investigations were made upon one type of carcinoma only—that with which the author has greatest familiarity—the adenocarcinoma of the stomach. A *résumé* of recent experiments on tumor transplantation preceded the writer's personal experiments, the main conclusion of which was that gastric ulcers can be experimentally produced, and that the edges of these gastric ulcers can be brought to undergo adenomatous transformation by the injection of a cell-free and sterile fluid obtained from a cancer of the same organ from the same species of animal.

Inasmuch as this filtrate was destroyed after being heated to 60° C., it was concluded that the agent active in causing this abnormal proliferation at the edges of experimental gastric ulcers was a catalytic agent. It might be objected here that the successful experiments were too small in number to permit of reliable conclusions. On this point I wish to state that the experiments extended through years, and at times had to be given up entirely for five to six months for lack of material, because I believed that I could work only with cancer material developed spontaneously in animals, and that cancers even if produced experimentally in the method described did not contain the catalytic agent in sufficient quantity to cause adenomatous proliferation in other animals. The main reason for this is to be sought in the fact that the experimental adenomata are very small; in three out of four cases their recognition depended upon microscopic examination. Although I was and still am in communication with the principal veterinary schools of this country, and even with Professor Ostertag and Professor Regenhogen, of the "Thierärtzliche Hochschule," of Berlin, I have come into the possession of only one dog with cancer of the stomach. The investigations would

have been indefinitely delayed had I depended exclusively upon this material. At present I am still engaged with these experiments, and by the aid of Profs. Frank Martin and J. Mason Hundley, whose aseptic technique I hope will secure me a larger number of recoveries from the operations described, I hope to be able to report an additional number of successful experiments in the near future.

The fact that in one instance adenomatous degeneration identical with ulcus carcinomatosum developed at the edges of a pre-existing gastric ulcer spontaneously gives promise of a new source from which to derive canine cancer material. At the same time this spontaneous development of cancer may be interpreted as a criticism of my deductions. It may be argued that the injection of the sterile and cell-free cancer extract does not prove that an enzymatic agent is necessary to start already proliferating cells into a condition of malignancy, for this instance proves that they may pass over into that state without any extraneous agency. Upon closer consideration, however, this criticism can hardly be considered as invalidating the main deductions, for throughout our considerations I have not argued that something entirely extraneous to the cell is needed to cause cancerous proliferation, but, on the contrary, I have tried to emphasize that the agent is something which the cell contains or produces within itself, but its regulatory mechanism is destroyed, etc.

The adherents of the parasitic theory might argue that the cancer extract, though sterile, may contain the products of bacterial metabolism, toxins, etc., which are soluble and can pass through a Pasteur filter, and that it is these toxins which acted as the agency causing the abnormal growth. This objection it is impossible to meet. It might be urged, however, as far as we can judge from the infectious diseases, that bacterial toxins may after injection cause the clinical picture of the disease, but not the characteristic histological alterations in the cells of the tissue which are concomitant with an infection by the living bacteria. Injections of tuberculin, for instance, cannot cause tubercles.

A possible objection is also found in the fact that adenomas of the digestive canal have been caused by mechanical injuries; for instance, by cutting off the lower ends of the glands of Brunner and of Lieberkühn. This observation has not as yet been satisfactorily investigated, and it has not been claimed that adenomas caused in this way were malignant. Lubarsch[1] succeeded in producing a fibro-adenoma in the liver by transplanting a portion of liver into an artificial lesion made in another region of this organ. He does not maintain, however, that this was a malignant—or, as he prefers to designate it, an "autonomous"—neoplasm, and presumes[2] that his experimental neoplasm would have eventually given way to a connective tissue cicatrix.

[1] Zur Lehre v. d. Geschwülsten, etc., loc. cit., p. 253.

[2] Loc. cit., p. 254.

In the preceding it has been pointed out that the autonomous development of neoplasms (adenomas) may be due to subtle damage to cytoplasm, which is in fact another way of expressing the traumatic and irritation etiology of neoplasms. I do not wish to dispute such possibilities. On the contrary they are to a large extent necessary for the bringing about of deranged catalytic action already described. It is important to emphasize in this connection that I have not succeeded in producing an adenocarcinoma by cutting or bruising the gastric glands, not even when they were in the environment of a pre-existing lesion.

The studies concerning the effect of osmotic pressures upon normal and cancer cells suggest the influence of physical energies upon normal as well as abnormal cell growth, and that future investigations along this line even promise to throw light upon this problem.

The immediate and specific causes of cell division are next considered. The theories of Virchow, Thiersch, Boll, and Weigert are abstracted, and the conclusion reached that the stimulus to normal cell growth is of a chemical nature.

The influence of physical laws upon cell growth constitutes another paragraph, which is followed by a consideration of the question of how the cell builds up protoplasm, that is, the methods and means by which it carries on the synthesis of its own substance. It is here suggested that this is effected by means of intracellular catalyzers.

The conception of how the cell protoplasm must be constructed, its possible chemical organization, concludes with a support of the view accepting the foam structure of protoplasm, and of a special catalyzer regulating the synthetic construction of protoplasm.

As the cell is conceived to be made up of innumerable ultra-microscopic compartments, the more subtle and partial damage of cytoplasm and nucleus in disordering the orderly and normal performances of intracellular catalysis are next set forth.

The reversibility of enzymes is then briefly considered, and the possibility of a damage to the ferment which controls the upbuilding of protoplasm is suggested, and also that there cannot be ubiquitous chemical equivalence of protoplasm.

In the final paragraph on metastases the suggestion is thrown out that possibly the blood serum contains defensive substances effective in the destruction of cancer cells, and the study of this means of defence gives hope of a more successful form of treatment.

In speaking of the transformation which the edges of the experimental ulcer in dogs underwent after injecting the sterile extract of canine gastric adenocarcinoma I may have unwittingly designated them as "gastric adenocarcinomas." What I really mean throughout the article is not that a genuine gastric carcinoma had been produced in my experiments, but that such a histological transformation was effected that the

microscopic appearance resembled that of a beginning adenocarcinoma. This expression is as far as the experiments justify me to go. I do not wish to imply that a typical cancer had been produced in this way, for this designation brings with it numerous attributes which it was impossible to bring into the experimental results. Above all things, I am not able to say whether the cell proliferation thus produced experimentally would have gone on to develop a genuine malignant tumor had the animals been permitted to live, or whether the proliferation would have been arrested and its place taken by a cicatrix. To complete the conception of carcinoma we must demand the evidences of malignancy, as is expressed in the production of metastases. Metastases were not produced in any of the animals examined. They occurred only in the dog in which a gastric ulcer had developed spontaneously.

RUBBER TISSUE AS A DRESSING.

By G. Tucker Smith, M.D.,
SURGEON, U. S. N.

In treating any lesion of the skin in which an ointment is indicated as a dressing, it is of prime importance that the parts should, first, be thoroughly protected from infection from without; second, the ointment used should be kept in constant touch with the parts; third, the dressings, when changed, should come away without sticking and without damaging the new-formed and delicate epithelium, and, fourth, that the dressing should be kept on as long as possible. All these requirements are admirably filled by rubber tissue. The parts having been cleansed with warm sterile water and green soap, should then be dried. The ointment is next spread on and covered over smoothly with sterile rubber tissue. Sterile lint is next applied and the whole secured with gauze bandage. Several cases are cited to illustrate its benefits:

F. J. McA., warrant machinist, U. S. N., aged thirty-three years, native of Brooklyn, N. Y., was, on November 24, 1902, while at work repairing a steam launch, severely scalded by escaping steam on both feet and wrists. The pain was severe, but was relieved by wet picric acid dressings and a hypodermic injection of morphine sulphate, one-quarter grain. The next morning it was found, on removing the dressings, that large blisters had formed. These were punctured, and the serum evacuated with aseptic precautions. A 10 per cent. boric ointment was then applied to the affected parts, and over this rubber

tissue, lint, and a bandage. The dressings were changed from time to time without adhering to the skin or causing pain. By December 3d he was well, the old skin having been entirely replaced by the new without infection.

Mrs. F. B., a young married woman, came under my charge last summer. She was suffering with a severe case of psoriasis. The disease had existed for almost two years, and had been very rebellious to the usual treatment of chrysarobin and collodion, locally, with arsenic internally. The eruption was confluent and covered the arms, forearms, the lower part of the body, the lower extremities, and the scalp. A 10 per cent. ointment of chrysarobin was applied to the arms and forearms with the rubber tissue daily. The improvement was prompt and gratifying. She had made for the body a jacket lined with the tissue. She moved to another locality early in October, but kept up the treatment faithfully. I heard from her from time to time that the eruption was gradually but steadily disappearing, and in January she wrote me that it had entirely gone, with the exception of a few small spots.

B. S., an infant, aged eight months, was recently treated by me for acute eczema of the scalp. The little fellow was suffering greatly from the itching and consequent loss of sleep. Rubber tissue was sewed into a tight-fitting hood of light cotton material. Zinc ointment (ʒss–ʒj) was applied, and the hood tied on closely and kept on day and night. The scalp was cleaned daily with sweet oil and the ointment and hood re-applied. The relief was evident, and in five days the eruption had disappeared.

In conclusion, I would state that doubtless this method has been used by others. As far as I am concerned it is original. I do not believe, however, that its advantages are generally known, and hence deem it worthy of report.

REVIEWS.

HANDBUCH DER PATHOGENEN MIKROÖRGANISMS.

HANDBOOK OF PATHOGENIC MICROÖRGANISMS. Edited by PROFS. W. KOLLE and A. WASSERMANN, with the collaboration of PROFS. BUCHNER, CORNET, EHRLICH, ARMAUER, HANSEN, KITT, H. KOSSEL, METSCHNIKOFF, A. NEISSER, NOCARD, WEICHSELBAUM, and others. Jena: Gustav Fischer, 1902.

FROM its great extent, its voluminous and widely scattered literature, and the increasing variety and novelty of many of its subdivisions, bacteriology is eminently fitted for encyclopædic treatment. Many books have been planned to this end, and some of them have been highly successful, but it is inevitable that a single volume cannot contain many details that even the general reader may wish to know. A more serious result in such books depends on the fact that the most indefatigable writer cannot keep up with all departments of the subject and give the essential part, well-digested, to the reader. The undertaking of Kolle and Wassermann seems well adapted to meet the need, both in size and plan, and in the collaboration of a large number of authors, all of whom are well known as investigators and writers, and many as discoverers or specialists of the first rank. The work is devoted especially to the micro-organisms important in pathology, including that of the lower animals. (Facts of general interest regarding saprophytic parasites are, however, considered in the chapter on General Morphology and Biology.) Methods of diagnosis and clinical and epidemiological data are to be thoroughly discussed, and a whole volume (the third) is to be devoted to the important subject of immunity. The whole is to appear in seventeen rapidly following fasciculi, with a quarto atlas in six fasciculi. The first instalments of text and atlas are most promising. Beginning with a brief but comprehensive general view of the historical development of "Infection, Immunity, and Prophylaxis," by R. Abel, "General Morphology and Biology" are taken up by E. Gotschlich. All the details of the subjects are discussed with great thoroughness, and, as is so useful in such a work, with references by number to original sources in connection with each statement, every section having a classified bibliography at the end. The second chapter is not finished in the one hundred and fifty pages it takes up in the first fasciculus. Each part is treated with admirable fulness. The sections on "Latent Infection," "Auto-infection," "Excretion of Infectious Organisms from the Body," and "The Sources of Infection" may be particularly mentioned as valuable alike to the general medical reader and the specialist, but the more recondite topics, such as metabolism of bacteria, enzymes and ferments and variability are equally well done. Dogmatism is safely avoided, and conflicting views, inevitable in the present

state of our knowledge, are fairly stated, though the author does not hesitate to give his own opinion. The text is illustrated with figures in black and colors. The *Atlas* is to be made up of photographs, partly from negatives by Prof. E. Zettnow, partly from those furnished by the several authors. The first fasciculus contains a short description of the technique by Zettnow, and two plates, with thirty-eight pictures, illustrating the morphology of various species, chiefly bacteria, with a uniform amplification of one thousand diameters. Though the pictures have not the artistic beauty of photogravures, they are all the better for the purposes of study and comparison. Altogether, the work promises to be a satisfactory as well as an indispensable one, useful to the student and the physician, as well as the professional bacteriologist and teacher. We note, with satisfaction, that investigations made outside of Germany are often referred to, and, as the parts treated in the first instalment deal with topics that have not been studied as much in America as have many others, there is every reason for believing that the numerous researches of American bacteriologists will be more adequately referred to than hitherto. The mechanical execution of the book shows the skill and care we have become accustomed to in the publications of Mr. Gustav Fischer. The price, about twenty dollars (single copies are not to be sold), is relatively low, and should assist in a wide distribution of the Handbook. G. D.

THE INTERNATIONAL TEXT-BOOK OF SURGERY, BY AMERICAN AND BRITISH AUTHORS. Edited by J. COLLINS WARREN, M.D., LL.D., Hon. R.F.C.S. Eng.; Professor of Surgery in Harvard Medical School; Surgeon to the Massachusetts General Hospital; and A. PEARCE GOULD, M.S., F.R.C.S., Surgeon to Middlesex Hospital; Lecturer on Surgery, Middlesex Hospital Medical School, etc. Second edition, thoroughly revised. In two volumes. Vol. I., General and Operative Surgery; Vol. II., Regional Surgery. Philadelphia and London: W. B. Saunders & Co., 1902.

THE exhaustion of the first edition of this work within two years speaks for its reception by the profession and by the medical schools. The changes and additions noticeable in this second edition are to be found particularly in the chapters dealing with military and naval surgery, the lymphatic system, and the spleen. Changes and improvements are also observable in the discussion of the surgery of the kidney. The work consists of two volumes, each containing about 900 pages. It is the labor of about sixty authors, English and American, all well known and eminently fitted to write the portions assigned them.

The first volume is devoted to general surgery and the second to special surgery. The various chapters are not signed by their respective writers, but a list of the chapters and their respective authors is to be found in the front of each volume. We feel that it would be an additional advantage to have the name of the writer appear at the head or at the end of each chapter, so that, without trouble, the reader could learn who wrote the portion of the book which he is consulting. The illustrations are particularly to be commended, not that they are exceedingly numerous, but because they are particularly good. There are nine full-page illustrations in colors. In the first volume we find but

few points for criticism, and many for commendation. The chapter on Fractures is the most generally acceptable brief treatise on fractures with which we are acquainted. We are glad to see an author who is willing to urge a departure from the old lines of treatment, which consisted in prolonged fixation and a postponement of any motion of the part for a number of weeks, and to substitute for these a more limited time of immobilization, followed by early movement and early massage. For fractures of the lower end of the humerus involving the joint, he advises only acute flexion, and in this we thoroughly concur. If his suggestions regarding the treatment of fractures at the lower end of the radius were followed there would be fewer cases of stiff wrists and finger joints following these injuries. In the treatment of fractures of the patella, too, particularly by the open method, it is shown that the old treatment of nearly interminable fixation is to be abandoned. We regret that the writer of the chapter on Injuries of the Joints has failed to make any mention of compression in the treatment of sprains, particularly of the ankle-joints, since we feel that no chapter on this subject can be complete without recommending this method of treatment, and more particularly that mode of compression known as the Gibney adhesive strip dressing. Dislocation of the hip-joint and diseases of this joint are given extensive consideration.

The chapter on the Heart and Bloodvessels is an excellent one, and the author's attitude toward the treatment of injuries of the heart appeals to us as essentially the right one, urging as he does, prompt surgical intervention in all cases of punctured wounds of the heart and pericardium.

The second volume, which deals with regional surgery, deserves a hearty commendation. Each subject is dealt with in a thorough manner by an author who has devoted much time and special attention to its study. It is this fact which makes us feel that the book is more valuable than one written by a single authority. The illustrations are in most respects new, and not the ones we are accustomed to meet with in every surgical work. One of the closing chapters of this volume deals with traumatic neuroses. This is a subject well included in a surgical work of this kind.

In closing we can say that we believe this work to be more generally satisfactory than any book of similar proportions. The second volume is especially valuable because of the excellent selection and assignment of authors. J. H. G.

General Paresis, Practical and Clinical. By Robert Howland Chase, A.M., M.D., Physician-in-Chief, Friends' Asylum for the Insane; late Resident Physician, State Hospital, Norristown, Pa.; member of the American Medico-Psychological Association; Fellow of the College of Physicians, Philadelphia. Philadelphia: P. Blakiston's Son & Co., 1902.

Dr. Chase has had a long and rich experience in studying and treating the insane, and it goes without saying that a book of his must be good. The expressed purpose of the book is to be a guide to the general practitioner, the man into whose hands the victim of paresis falls long before he is seen by the specialist, the man who alone has an opportunity to help him. It is vitally important that the family doctor should know

and thoroughly know the symptomatology of paresis, for on its early diagnosis hangs the possibility of amelioration. Dr. Chase gives a very good account of the disease. His work is almost wholly clinical. He dwells but little on morbid anatomy. In the clinical histories he uses no cases of his own, but quotes from the literature. The reason for this is manifestly a kind desire not to run the risk of hurting the feelings of relatives of his patients. The effect may be, however, to make some readers who are unacquainted with him think that he is one of those youngsters just out of college who, seized with the ambition to be great, make a book with the scissors. We need not say this is not a scissors book. The data are from the world at large; the opinions are from Dr. Chase, and are based on his knowledge and his experience. Physicians in general practice look askance at books on special subjects. They expect to find a strange vocabulary and obscure discussions on subjects either obscure in themselves or made so by the writers. They sometimes find what they expect. In Dr. Chase's book they will find a clear and simple account of general paresis. They will also learn what can and cannot be done by treatment. These things are worth knowing.

C. W. B.

DISEASES OF THE STOMACH: THEIR PATHOLOGY, DIAGNOSIS, AND TREATMENT, WITH SECTIONS ON ANATOMY, PHYSIOLOGY, CHEMICAL AND MICROSCOPIC EXAMINATION OF STOMACH CONTENTS, DIETETICS, SURGERY OF THE STOMACH, etc. Pp. 894. By JOHN C. HEMMETER, M.D., Ph.D., with many original illustrations and a lithograph frontispiece. Third enlarged and revised edition. Philadelphia: P. Blakiston's Son & Co., 1902.

DR. HEMMETER is to be congratulated upon maintaining the high standard of excellence manifested in the first edition of this attractive volume, the most important and comprehensive treatise on the subject in the English language. The general scheme of the work is that indicated by the sub-title, and each section, whether devoted to the anatomy and physiology of the stomach, to analysis of the stomach contents, to the diagnosis and medical treatment of the various gastric ailments, to the diet kitchen, or to the surgery of the stomach, is attractively developed and brought up to date. It is the author's plan to present an elaborate treatise, whence appears a good deal which would be superfluous in a less pretentious volume devoted rather to an exposition of personal experience and a presentation of the gist of the subject than to a detail, as is here done, of not only what is essential in apparatus and of approved value in treatment, but what may be of little utility to either the specialist or to the general practitioner. Here the subject is intended to be presented in what may be called encyclopædic form, and this detail seems rational if, at times, it may be vexatious to the reader.

The volume is increased by nearly one hundred pages over that of the first edition. This last received an extensive review in these columns, and the faults there noted, inseparable from the primary production of such a work, have practically all been eliminated. We may say that in glancing over the work we see little to condemn and much to praise.

It must be said it is regrettable that Dr. Hemmeter cannot offer a more certain remedy than ergot for the control of "copious and persistent" hemorrhage occurring in gastric ulcer, and that, indeed, in this particular he still pins his faith to this drug, even though its use has, as he remarks, the indorsement of Riegel, Ewald, and Nothnagel. As the reviewer has insisted upon in several publications (see, especially, *System of Practical Therapeutics*, vol. ii., p. 949, Lea Bros., 1892) in the past ten or more years, ergot is contraindicated rather than of value in hemorrhage from ulcer requiring active treatment, that of copious extent and often of persistent form, then due commonly to arterial erosion and not to capillary oozing. In frank hemorrhage thus occurring, ergot, from its well known power of causing constriction of the arterioles and not of the larger vessels, thus raising resistance *a fronte*, is likely, if it has any effect at all, to augment the bleeding. The reviewer has never observed any benefit from the use of ergot in hemorrhage of this character. We think Dr. Hemmeter might well have mentioned the utility of calcium chloride by enema or by hypodermoclysis and of gelatin similarly used in recurrent hemorrhage. It is on one or both of these agents rather than on ergot that the physician must rely.

It is a pleasure to note Dr. Hemmeter's view as to the status of the abused employment of electricity in diseases of the stomach. The results of Hemmeter's experiments are in line with Meltzer's and others, that the gastric muscularis is unresponsive to direct faradic and galvanic stimulation as it is therapeutically employed in diseases of the stomach. These laboratory experiments are supported by past extensive use of this remedy by the writer. Beginning its employment in 1890, through the teaching of Einhorn, after some years' thorough trial of electricity in all classes of cases in which it seemed theoretically indicated, the reviewer's final judgment was that its utility is narrow, and, though he still employs it discriminately, he does not use it with the notion of influencing gastric motility through direct effect on the stomach muscles. He has never been able to satisfy himself that by either galvanism or faradism could the capacity of an anatomically-dilated stomach be reduced. It is not long since that a still verdant, though active, laborer in the field of "gastro-enterology," in an article on the subject, related cases in which but an application or two of intragastric electricity had a noteworthy effect (susceptible of demonstration) in diminishing the capacity of a dilated stomach and raising its inferior curvature.

We are not altogether in agreement with Dr. Hemmeter as to the utility of HCl employed as he recommends it for its digestive effects in cases of absence of the gastric secretory function—achylia gastrica. The amount of HCl required for proteolysis, discussed by Dr. Hemmeter in another section of the work, would indicate the inefficiency of the dose suggested in achylia—one drachm of the dilute acid in divided portions after meals. This dose, though efficient in cases of mere subacidity, can be of no practical utility with complete absence of gastric secretion. One drachm of the dilute acid is approximately equivalent to 190 c.c. of 0.2 per cent. HCl, and this is far and away inefficient for satisfactory saturation of the proteids of an ordinary meal. As calculated by Blum and confirmed by Chittenden and others, including the reviewer, with a daily consumption of 100 grammes of dry proteid, some 4500 c.c. of 0.2 per cent. HCl is required, and with this there would be no excess appreciable of free acid. With the employment of HCl, as a digestant

in achylia, pepsin must, of course, be coincidently administered, unless it is merely desired to form acid albumin. The writer, after extensive trials of HCl, both to promote a return of its own secretion and as a digestant, in a series of carefully studied cases of achylia, some years ago abandoned its use as impracticable other than when employed as a stomachic. It is in cases of achylia gastrica that real digestive effects are obtained from an active preparation of papain or of the pancreas. Fresh pineapple juice, mentioned by Hemmeter, although of similar value, is less practicable for continuous administration. In at least two of the reviewer's cases he noted decided interference with the digestive function of the stomach under the HCl therapy. In each case chymifaction was apparently accomplished through the conservative regurgitation of intestinal (pancreatic) juice into the stomach. HCl may, however, be employed as a stomachic or as a stimulant to the return of its own secretion (in nervous anacidity), administered either alone or in combination with vegetable bitters, but then is most efficient given on the empty stomach; then only can sufficient be administered, except after a very moderate meal, to exert an antiseptic effect.

In conclusion, we again congratulate Dr. Hemmeter on his excellent treatise, which we unhesitatingly recommend to those interested in the subject.

D. D. S.

STUDIES OF THE INTERNAL ANATOMY OF THE FACE. By M. H. CRYER, M.D., Professor of Oral Surgery, Department of Dentistry of the University of Pennsylvania. Philadelphia: The S. S. White Dental Mfg. Co., 1901.

THIS book might well be called an atlas of the anatomy of the bones of the face, accompanied by a running comment on the general principles of their pathology and surgery. Probably the same modesty which induced the author to give his work such an unostentatious title has likewise led him to condense the really wonderful amount of valuable information which it contains within such a limited number of pages. The value of a monograph of this character cannot be estimated by its size. In Dr. Cryer's book there is not a paragraph which could be omitted without the loss of something of distinct value to teachers and students of the anatomy of the head. Of the illustrations, every one of them is original in this work, and too much cannot be said in their praise. They are pictures of specimens, and, having been made by the author himself, they show the points which he really wished to elucidate. In the course of his work Dr. Cryer has discovered many new and important points in the osteology of these bones, particularly as regards the course of the various nerves which are found pursuing their way through so many of them. Many instances might be brought forward to show in what way the heretofore received ideas as to the regional anatomy of the face are disturbed by Dr. Cryer. For instance, we would direct particular attention to his studies of anatomy of the inferior dental and the infraorbital nerves. This important monograph of Dr. Cryer's should be in the hands not only of every student of anatomy, but of every dental surgeon and rhinologist. Its practical value can hardly be over-estimated.

F. R. P.

CLINICAL PSYCHIATRY. A TEXT-BOOK FOR STUDENTS AND PHYSICIANS. Abstracted and adapted from the sixth German edition of Kraepelin's *Lehrbuch der Psychiatrie.* By A. ROSS DEFENDORF, M.D., Lecturer on Psychiatry in Yale University. The Macmillan Company, 1902.

THE purpose of this book is twofold—to make the views of Kraepelin more accessible to American readers and to provide a concise text-book. The author has succeeded. The book opens with a section on general symptomatology, after which the various forms of mental disease are studied in order. There is a short account of idiocy and imbecility at the end. The article most interesting to us is the one on dementia precox. Cretinism, even in an American book, deserves more than two pages. There is a short bibliography at the end of each subject, in which only important papers are mentioned—a bibliography for use and not to impress the reader with the author's erudition. The descriptions of disease are clear, the English concise and not verbose, and there is an absence of non-understandable words sometimes met with in books. Dr. Defendorf makes no attempt at classification; he has no chapter on that subject and he deserves thanks therefore. In the present state of knowledge no consistent classification of mental diseases is possible, and an inconsistent classification is useless. Altogether the book is admirable, and we advise every student, undergraduate or graduate, to study it.

C. W. B.

MEDICAL MICROSCOPY: DESIGNED FOR STUDENTS IN LABORATORY WORK AND FOR PRACTITIONERS. By T. E. OERTEL, M.D. 8vo., 362 pp., with 131 illustrations, some of which are colored. Philadelphia: P. Blakiston's Son & Co., 1902.

THIS little book is a straightforward presentation of the branches of medical science for which a knowledge of the microscope and its teachings is essential. It makes no claim at fulness or authority, and is designed for the practitioner and the student who are deprived of the advantages of laboratory training. When it is seen that a description of "The Microscope," "Fixation of Tissues," "Bacteria," "The Blood," "Urine," and the various fluids of the body are covered in the headings, one is rather amazed that the author has made a book that is so readable and accurate within its limitations. We are a bit skeptical as to the necessity for such a treatise on the ground of "a little knowledge;" but, granted the necessity, the accomplishment is more than creditable. The illustrations are good and help the text.

F. P. G.

A MANUAL OF GENITO-URINARY AND VENEREAL DISEASES. FOR THE USE OF STUDENTS AND PRACTITIONERS. By LOUIS E. SCHMIDT, M.D., of the Chicago Polyclinic. In one handy 12mo. volume of 250 pages, with 21 illustrations. Philadelphia and New York: Lea Bros. & Co., 1902.

THIS little volume, one of the medical epitome series, aims, in the words of the author, "to afford a comprehensive survey within a com-

pact space." Although, as a rule, we question the utility of such works to the practitioner who is really in search of information, this epitome is exceptional in the amount of really valuable material which it offers. It is to the medical student, however, who seeks to attain the most information in the briefest possible time, that the present book will prove especially useful as an aid in the lecture-room and a supplement to larger works. As far as consistent with the small space devoted to the subject, the treatment of the various genito-urinary and venereal affections is fully given and is thoroughly up to date. H. M. C.

THE AMERICAN YEAR BOOK OF MEDICINE AND SURGERY FOR 1903: A Yearly Digest of Scientific Progress and Authoritative Opinions in All Branches of Medicine and Surgery. Arranged with critical editorial comments by eminent American specialists, under the editorial charge of GEORGE M. GOULD, A.M., M.D. In two volumes. Volume I., General Medicine, fully illustrated. Volume II., General Surgery, fully illustrated. Philadelphia, New York, London: W. B. Saunders & Co., 1903.

THE *American Year Book* is once more before us, and fully maintains the high standard of excellence which has given it its reputation in previous years. It is impossible in a work of this character to pick out any particular department for special notice, as the various sub-editors, under the able supervision of Dr. George M. Gould, have all of them performed their work in so uniformly excellent a manner that the choice of any one of them for particular commendation would be invidious. During the temporary lapse of the *Index Medicus* books of this character have been compelled to serve in its place, but even with the reincarnation of that invaluable periodical such a work as the *Year Book* will continue to remain an indispensable adjunct to the library of every scientific man, because in no other way can he attempt to familiarize himself to any extent with the current medical literature. F. R. P.

PROGRESSIVE MEDICINE. A Quarterly Digest of Advances, Discoveries, and Improvements in the Medical and Surgical Sciences. Edited by HOBART AMORY HARE, M.D., Professor of Therapeutics and Materia Medica in the Jefferson Medical College of Philadelphia; Physician to the Jefferson Medical College Hospital; Laureate of the Royal Academy of Medicine in Belgium, of the Medical Society of London, etc. Assisted by H. R. M. LANDIS, M.D., Assistant Physician to the Out-Patient Medical Department of the Jefferson Medical College Hospital. Volume IV., December, 1902. Philadelphia and New York: Lea Brothers & Co., 1902.

THE December volume of *Progressive Medicine* contains the recent literature on the Diseases of the Digestive Tract and Allied Organs, arranged by Einhorn; Anæsthetics, Fractures, Dislocations, etc., by Bloodgood; Genito-urinary Diseases, by Belfield; Diseases of the Kidneys, by Brad-

ford; Physiology, by Brubaker; Hygiene, by Harrington; and Practical Therapeutic Referendum, by Thornton. It is useless to say anything regarding the style and standing of *Progressive Medicine*. It has already won for itself an enviable place in medical literature.

The volume before us contains liberal abstracts on the subjects under discussion and excellent critical remarks by the various editors. The first portion of the book, although prepared by a medical man, will be found of particular interest to surgeons as well as to physicians, since it deals with the various pathological lesions of the whole alimentary canal, in the treatment of which the surgeon and physician are so frequently associated. The use of the œsophagoscope, for instance, is explained and illustrated. Diverticula and dilatations of the œsophagus are also discussed. Recent literature on hour-glass stomach, perforation of the stomach, and appendicitis is also dealt with in this portion of the volume. The literature on hemorrhage, surgical shock, and fractures is particularly well presented.

It is impossible to refer to all the various chapters, but it can be said that this volume is in keeping with the standard of its predecessors, and will be found of great value to anyone wishing to acquaint himself with the latest literature on the subjects here presented. J. H. G.

Clinical Methods: A Guide to the Practical Study of Medicine. By Robert Hutchison and Harry Rainy. Fifth edition. Chicago: W. T. Keener & Co., 1902.

Besides being a repository of clinical laboratory methods and of the numerous instruments of precision, familiarity with which is now required of every student, the book is really an excellent and trustworthy manual of physical diagnosis. That portion of the book, in fact, comprising about one-third, distinguishes it very favorably from many more pretentious works on the same subject. Precision of statement and lucidity of style—indispensable conditions of a successful didactic work—are conspicuous features, while a judicious selection of diagrams illustrating physical signs and the logical classification of phenomena add to its practical usefulness. The index also deserves a word of commendation. Theoretical discussion and interpretation of phenomena are purposely reduced to a minimum, but perhaps a little more liberality in this respect would have proved acceptable to the reader; instead, the pruning-knife might have been applied a little more vigorously in the choice of clinical instruments from among the great number that compel selection. Some of these might well be spared in a practical manual for students; we refer particularly to blood pressure instruments, the uncritical presentation of which must prove misleading to anyone who has not had personal experience with these devices. In spite of the authors' disclaimer of any attempt at completeness in the list of laboratory methods included in the volume, the latter will be found to contain all those that are essential and practical, and leave a margin for personal preference. Four editions have been exhausted since the first appearance of the book five years ago, and we sincerely hope the success of the fifth will be equal to that of its predecessors. R. M. G.

LES DIFFORMITÉS ACQUISES DE L'APPAREIL LOCOMOTEUR PENDANT L'ENFANCE ET DE L'ADOLESENCE. Par le DR. E. KIRMISSON, Professeur de clinique chirurgicale infantile à la Faculté de médecine, Chirurgien de la hôpital Trousseau, Member de la Société de Chirurgie, Membre correspondent l'American Orthopedic Association. Avec 430 Figures dans le Texte. Paris: Masson et Cie, 1902.

A PRIMARY anatomical scheme of classification, with subdivision of chapters from the pathological viewpoint, is that used in most works of orthopedic surgery. The treatise of Young was the first, in our knowledge, to depart from this precedent. Its primary divisions are partly devoted to lesions of the individual tissues and partly to an etiological and pathological classification of the subject.

It is from the latter and more scientific standpoint, that of the etiologist and pathologist, that Kirmisson has divided the 645 octavo pages of the volume under review into four books, entitled as follows: I. Tuberculosis. II. Rickets and Sequent Troubles of Development during Infancy and Youth. III. Deformities Sequent to Affections of the Nervous System. IV. Deformities of Traumatic and Inflammatory Origin. These books are subdivided into chapters with anatomical headings. It is interesting to note that the author has placed the greater part of his remarks upon scoliosis in the book devoted to rickets.

Excellent and profuse pen-and-ink drawings, some radiographs, and a few half-tones admirably illustrate not only the pathology of the lesions described, but also most serviceable mechanical aids in the accurate record and successful treatment of acquired deformities. The author is to be no less congratulated on the wide scope of this volume, written from the limits of personal experience than on the practicality and cosmopolitan character of the appliances he commends. The book is notably free from the elaborately impossible contrivances that often astonish the American reader of German works on surgical topics. The paper and typography are all that could be desired. The binding is of paper, and as is unfortunately the rule with French books, an alphabetical index is omitted.

To the student, the general surgeon, and to the orthopedist especially, this should prove a most serviceable volume. J. M. S.

LECTURES ON CHEMICAL PATHOLOGY IN ITS RELATION TO PRACTICAL MEDICINE. Delivered at the University and Bellevue Medical School, New York City. By C. A. HERTER, M.D., Professor of Pathological Chemistry, University and Bellevue Medical School, New York. New York and Philadelphia: Lea Brothers & Co., 1902.

DURING the last few years modern methods of scientific study have thrown the most astonishing light upon certain chemical changes which take place in the body cells both in health and disease—changes which are quite as important as the pure morphological alterations of the cells. Certain phases of pathology and chemistry have thus come to overlap, and in consequence there result the problems of chemical pathology. Dr. Herter's book cannot be too highly praised. The subject, intensely interesting in itself, derives a double value from the

manner in which it is presented, and although dealing principally with experimental medicine, forms a sound basis for the application of certain principles to practical medicine. The volume is divided into thirteen lectures. The first, which forms rather an introduction to the general subject, treats of the chemical defences of the body against diseases, and includes a short review of the bacteriolytic actions of the body fluids as well as the manner in which the body cells contrive to rid the body of chemical toxins. Then follow four lectures on the chief food-stuffs and their fate in health and disease, while two more lectures are devoted to a discussion of excessive fermentation and putrefaction in the digestive tract, and one each to the chemical pathology of gastric and intestinal digestion. The tenth and eleventh chapters deal with the chemical pathology of hepatic diseases, and the twelfth, a most important one, with diabetes. The book ends with a discussion of starvation, under-nutrition, and obesity. Each subject is gradually expanded and developed, so that the more complicated processes are introduced by the simpler ones, and thereby become clear and are easily understood. When theories are advanced they are based upon sound experimental evidence, and the latest researches which have any bearing upon the subject are freely made use of. Indeed, much of the subject-matter can be found in no other text-books, and is compiled from very recent original literature. One of the many excellent features of the book is the short bibliography appended to each lecture, in which are given a few of the most important references on the subject under discussion. The book is well written, and the valuable material which it contains is read with pleasure. W. T. L.

A Text-book of Materia Medica, Therapeutics, and Pharmacology. By George F. Butler, Ph.G., M.D., Professor of Materia Medica and Therapeutics in the College of Physicians and Surgeons, Chicago, Medical Department of the University of Illinois, etc. Fourth edition, thoroughly revised. Philadelphia and London: W. B. Saunders & Co., 1902.

It is with much satisfaction that we take up this edition of Butler. It appeals to the student because it is systematic and thorough, and to the physician in that it contains in readily accessible form a large amount of material. The present edition differs from its predecessors in showing considerable rewriting, more confidence in some therapeutic measures—perhaps the result of more extended experience—and a longer list of remedies. In particular the results of laboratory work have been fully utilized to amplify the matter contained in "Physiological Action," and the journals devoted to therapeutics—of ever-increasing value and possibly number—have been drawn upon to fill out "Therapeutics." And in the process some ancient statements from hereditary text-books have lapsed into deserved oblivion. Thus the fourth edition comes much nearer to our ideal than did the first, six years ago. This volume should be held in high regard if for no other reason than that it lays so much stress on the untoward as distinct from the poisonous action of drugs, and the tables, pp. 48 to 53 inclusive, as well as the

preliminary statements, are too important to the practitioner to be passed without comment. Of information in which many text-books are still deficient, organotherapy and serum therapy may be cited as satisfactory in quantity and value of statements contained. The question of the day, "The Relation of Physical Chemistry to Pharmacology and Therapeutics," has been intrusted to Dr. Martin H. Fisher, who has developed it in a little over eight pages. As a well-arranged, classified, and comprehensive treatise on materia medica and therapeutics and some cognate subjects of importance to students, written in a clear and convincing style, we commend this as we have the other editions. The many items in which we noted improvements over its predecessors verify the claim of its thorough revision, and in this the valuable assistance of Dr. Smith Ely Jelliffe is acknowledged by the author. We congratulate the author on the realization of his desire to make the fourth in every way worthy of the success of the earlier editions.

R. W. W.

Physical Diagnosis: Diseases of the Thoracic and Abdominal Organs. By Egbert Le Fevre. Philadelphia and New York: Lea Brothers & Co., 1902.

A book, we think, of permanent utility to the student and practitioner of medicine has appeared in Le Fevre's *Physical Diagnosis*. It is one of the best works of its size upon this subject we have as yet seen.

Recognizing the necessity of a thorough understanding of those factors to which the production of physical signs are due, in order that the facts elicited may be properly interpreted, the author has spared no pains in showing their basis and underlying principles, and has illustrated the subject with numerous original cuts and photographs. In addition to the usual subjects treated of in the text-books of this character, there is appended a chapter on Examination by Means of the X-ray, a method of diagnosis which has proved of such substantial value in many otherwise obscure conditions that the subject can no longer be ignored in up-to-date medical books.

Considering that the work is in its first edition there are but few typographical errors, and while exception might be taken to some statements made in it, yet on the whole the volume may be heartily indorsed as a valuable addition to the library of the practitioner or student.

G. W. N.

Saunders' Question Compends, No. 25. Essentials of Histology. By Louis Leroy, B.S., M.D., Professor of Histology and Pathology in Vanderbilt University, Medical and Dental Departments, etc. Second edition, revised and enlarged. Pp. 263, with 92 illustrations. Philadelphia and London: Wm. B. Saunders & Co., 1902.

A second edition within a short period would indicate that this book meets and supplies a demand. The text is a concise and in the main accurate epitome of the subject, yet not so concise as to lose in clear-

ness. The new photomicrographs are a valuable addition to the book, and it is to be hoped that they will stimulate the author, in the event of further editions, to replace or improve the original sketches which appear crude in contrast. F. P. G.

A Text-book of Anatomy, by American Authors. Edited by Frederic Henry Gerrish, M.D., Professor of Anatomy in the Medical School of Maine, Bowdoin College. Second edition, revised and enlarged. Philadelphia and New York: Lea Brothers & Co., 1902.

The first edition of this work won for it a place among the very best of our general descriptive anatomies. This second edition shows a number of improvements over the first, particularly the chapter on osteology, to which has been added a number of excellent colored drawings, and the six contributors are to be congratulated on this excellent volume. One fact strikes the reader throughout, and that is that the book is written to teach. It is not composed of a mass of dry facts monotonously set forth, but the subjects are each made as interesting and comprehensive as possible. An excellent introductory chapter of twenty pages by Gerrish gives the student an idea of what anatomy is, and how it should be studied. Every student should read repeatedly the author's instructions regarding the method of study. It is this which is most essential, and which is most usually wanting in medical students. Another feature of this book which appeals strongly to us is the great number of excellent illustrations. What the student needs in studying anatomy in the absence of the cadaver is pictures and diagrams, which help him to comprehend and remember what he reads. In this respect we feel that the work before us surpasses any other with which we are acquainted.

The nervous system, always a difficult subject for the student, is set forth in the clearest and simplest manner, and beautifully and thoroughly illustrated. One of the closing chapters deals with relational anatomy, and is illustrated by a number of cross-sections of different portions of the body and photographs showing surface markings. At the end of the volume, also, are to be found a dozen skiagraphs showing the normal osseous system.

In his preface the editor thanks his publishers for their "remarkable liberality" in the matter of illustrations. Certainly they have been liberal; but, as we have said before, this matter is such an important one in a book of this nature that we feel the publishers have shown discretion as well as liberality.

In closing this review we feel that we can recommend this text-book of anatomy by American authors as probably the most generally satisfactory book of its kind and size published in recent years. J. H. G.

PROGRESS

OF

MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF

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An Epidemic of Paratyphoid Fever. De Feyfer and Kayser (*Münchener medicinische Wochenschrift*, 1902, vol. xlix. pp. 1692, 1752) report a carefully studied epidemic of paratyphoid fever occurring in the practice of the former, at Eiberg, in Holland. The epidemic consisted of fourteen cases, one of which was apparently a mixed infection with typhoid fever. The cases were characterized by a short prodromal stage of one to four days, with irregular elevations of temperature, loss of appetite, and pain in the head, back, and legs. The course was favorable in all cases, and there were no very serious sequelæ. The acutely infectious nature of the malady was undoubted. The temperature curve was typical in the mild as well as in the severer cases. There was a remittent and intermittent period. In the remittent period, both morning and evening exacerbations were occasionally to be made out. Sometimes the fever fell critically. The case of mixed infection with typhoid had an afebrile course. The pulse in general bore a direct relation to the height of the temperature. With regard to the intestinal tract, there were at the beginning of some cases vomiting and borborygmi; the tongue was almost always more or less coated; there were abdominal pains, though there was no tenderness on pressure. An ileocæcal murmur was always to be made out. The spleen was, as a rule, not palpable, but enlargement was to be made out by percussion. There was almost always diarrhœa, followed sometimes by constipation. The stools were thin, yellowish, and foul-smelling. The urine was, for the most part, free from albumin. In all cases examined for that purpose there was a diazo reaction and increased quantity of indican. The sensorium was generally clear, though the patients were sometimes somnolent and apathetic. A roseola was made out in half of the cases. The blood serum of the patients in all cases agglutinated paratyphoid bacilli of the type β of Schottmüller. Bronchitis was a common

complication. Angina was often observed at the beginning of the disease. In a few instances there was slight intestinal hemorrhage.

The authors review the work of Schottmüller, Kurth, and Brion, and Kayser, who have distinguished two types of paratyphoid bacilli, the second type, the organisms of which were agglutinated by the serum of these cases, being far the commonest.

Blood cultures were negative, possibly because but small quantities of blood were taken. The authors point out the fact that paratyphoids are not so remarkably rare, having been found in 6.6 per cent. of 180 cases of what was clinical typhoid fever by Schottmüller and Kurth.

The cases reported by de Feyfer constituted a definite endemic, resembling in all respects a mild typhoid fever. Such cases must be distinguished (1) from typhoid fever; (2) from the typhoid form of influenza; (3) from gastro-intestinal catarrh, with or without fever. The similarity with typhoid fever is so great that "the differential diagnosis as to whether typhoid or paratyphoid is present is impossible on the basis of clinical observation alone." The agglutinative reaction settles the question. There was reason to believe from the observation of this epidemic that the water from the River Berkel was, in some instances, the source of infection.

The authors conclude that "we have in paratyphoid fever evidently a widespread typhoid-like acute infectious disease which may, under similar etiological conditions, occur as does typhoid fever under the form of an epidemic.

"The cases so far observed have had a favorable course.

"Paratyphoid fever must, in our opinion, be treated from a hygienic-sanitary standpoint just as typhoid fever; that is, it is in the interests of public health to insist that the cases be reported and subjected to the same rules of disinfection as in typhoid fever.

"The diagnosis of paratyphoid is to be made by the help of the agglutination test or by cultivation of the bacteria."

On the Circulatory Disturbances in Collapse in Acute Infectious Diseases.—Passler and Rolly (*Münchener medicinische Wochenschrift*, 1902, vol. xlix. p. 1737), from Curschmann's clinic, contribute some extremely interesting observations upon the physiology of the circulatory disturbances occurring in collapse in acute diseases. The object of their investigation was to clear up the question, so important from a therapeutical standpoint, as to whether the circulatory collapse occurring under these conditions is due to cardiac weakness or to vasomotor paralysis, or to both. Von Stejskal and Waller estimated the functional capacity of the heart by comparing the carotid pressure with that in the left auricle. If the fall in carotid pressure be due to vasomotor paralysis rather than to weakness of the heart itself, the auricular pressure will also fall, while on the other hand, if the arterial pressure falls on account of the cardiac weakness, the auricular pressure will rise. Pässler and Rolly found that by extirpating the splanchnic nerve on both sides in rabbits a practically complete vasomotor paralysis follows, though, as a rule, the carotid pressure falls more than the auricular pressure, indicating that the heart works under somewhat more unfavorable conditions than ordinarily. If in such a case, however, abdominal massage be carried

out, or compression be made upon the aorta above the diaphragm, it is found that the heart is abundantly capable of carrying out the extra work put upon it. Such a heart, however, after a relatively short period of time, becomes gradually insufficient. That this insufficiency is probably due in great part to the deficient nourishment of the heart wall, due to the vasomotor paralysis, was shown by the fact that by large injections of salt solution into the jugular vein the carotid pressure was materially raised, while the action of the heart improved so that in some instances there was an actual increase of power above that previously following compression of the aorta. The authors believe that they have a measure of the functional power of the heart in the quotient between the auricular and carotid pressures when increased demands are brought upon the organ, as for instance, by abdominal massage or aortic compression. These methods the authors have utilized to determine whether the fall of blood pressure coming on at the height of diphtheria and pneumonia depends upon cardiac weakness or upon vasomotor paralysis. In experiments upon animals poisoned with diphtheria toxin they were able to show that the collapse depended always upon a diminution in the response of the vasomotors to sensory stimulation, while by the employment of aortic compression or abdominal massage the power of the heart was found to be rather increased than diminished. In some cases in which the reflex excitability of the vasomotors was entirely lost, the functional capability of the heart was found to be actually accentuated. Only gradually, at varying periods of time after this, did evidences of actual cardiac weakness develop. In the same manner as after splanchnic extirpation, the power of the heart even under these conditions might be sustained for a considerable length of time by very large infusions of sodium chloride. Similar conditions were observed in pneumococcus infections.

Portions of their conclusions are worthy of quotation. "The circulatory disturbances which occur at the height of various acute infectious diseases depend upon a paralysis of the vasomotors. The heart plays no part in the production of the fall of blood pressure occurring in the collapse. Increased work on the part of the heart may retard the dangerous fall of the arterial pressure for a time. When, finally, the blood pressure falls, the heart is secondarily damaged."

The authors, however, find evidence that the diphtheritic poison does exercise a direct influence on the heart muscle, though a similar condition was not to be made out in pneumonia. "It is not impossible that this diminution in the power of resistance of the diphtheria heart favors and hastens the oncome of secondary heart weakness in vasomotor paralysis. The heart in diphtheria, however, does not contribute toward the development of the circulatory disturbance which comes on at the height of the infection."

[The possible clinical importance of these interesting observations is evident. Such studies as these emphasize the necessity of more systematic and accurate records of the variations in blood pressure in acute febrile diseases than have been heretofore customary in most clinics.—W. S. T.]

The Nature of Non-tropical Chyluria.—FRANZ and VON STEJSKAL (*Ztschr. f. Heilkunde*, 1902, Band xxiii. (N. F. Bd. iii.), Heft 11, Abth. F., Heft 4, p. 441) contribute a valuable inquiry into the nature of the chyluria

of temperate climates. After a careful study of forty-one cases of non-tropical chyluria, all that they have been able to collect from the literature, to which they add a minutely studied case of their own, and a discussion of the theories heretofore advanced to account for this condition, they reach conclusions some of which are worthy of reproduction.

European chyluria forms, as does the tropical variety, a perfectly sharp disease picture not to be confounded with other affections. Of the two conditions brought forward as different characteristics, namely, the presence of parasites in the urine, as well as the appearance of hæmaturia in tropical chyluria, their absence in European chyluria, the first alone actually exists, the presence of parasites. The second point is not sufficiently important to be of weight in suggesting a difference in the cause of the two affections, especially inasmuch as the authors find that in the European form of the disease blood corpuscles have been made out microscopically in all cases, while in one the admixture of blood was evident macroscopically.

The similarity of the changes in the urine in both forms of the disease speaks in favor of a like cause. Their own observations in one case of European chyluria show absolutely no differences from the conditions found in the more common tropical form. These observations the authors believe to have resulted in a demonstration of the following facts:

"(1) The dependence of the chylous change in the urine upon the introduction of fat into the intestinal canal, proven
  (*a*) by the disappearance of the fat in the urine under starvation;
  (*b*) by the appearance of fat-free urine under a diet very poor in fat;
  (*c*) by the excretion of specific fats, such as olive oil colored with Sudan red, erucin, lipanin, by the urine following their introduction into the gastro intestinal tract;
  (*d*) by the circumstance that fat which is with difficulty absorbed appears in the measure of its absorbability.
(2) The lack of relation between the excretion of fat in the urine and its introduction by other methods, as, for instance, by subcutaneous introduction of colored fat.
(3) The early appearance of alimentary glycosuria, caused, probably, by the increased quantity of sugar in the chyle, resulting from the great amount in the intestinal canal.
(4) The appearance of chiefly mononuclear leucocytes in the chylous urine."

Their observations lead them to believe that the chylous character of the urine is to be regarded as the result of an actual mixture of chyle with the urine, and they point out the fact that in two instances of European chyluria a lymphatic obstruction was made out. The autopsy in Ponfick's case shows that a dilatation of the thoracic duct and of the intra-abdominal lymph vessels may, even in the absence of parasites, be associated with a chylous condition of the urine, the obstruction to the flow of lymph resulting eventually in the entrance of chyle into the lymphatics of the kidney or other parts of the uropoietic system.

They conclude that both European and tropical chyluria are the result of passive congestion of the chyle passages with consequent entrance of chyle into the uropoietic system.

SURGERY.

UNDER THE CHARGE OF

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An Operation for the Radical Cure of Aneurism Based upon Arteriorrhaphy.—MATAS (*Annals of Surgery*, February, 1903) states that in the operation that he has proposed the sac is, as a rule, not extirpated nor disturbed, except in so much as is required to evacuate its contents and freely expose its interior, and in this way it may be regarded as a derivative of the old Antyllian operation. Apart from this it differs essentially from either of the classical procedures in the fact that no ligatures are applied to the main artery, and that the circulation in the sac is arrested and hæmostasis is secured solely by suturing the arterial orifices found in the interior of the sac. Again, in suitable cases—that is, in the true sacciform aneurisms with a single orifice of communication with the parent artery—this method will allow the operator to obliterate the aneurism without obstructing the lumen of the artery or interfering with the circulation in the injured or diseased vessel, a great desideratum which should never be lost sight of when operating upon this class of cases. Finally, it differs essentially from the Antyllyian operation in the fact that the cavity of the sac is not simply packed or drained and left to heal by granulation, but is at once obliterated by inverting or infolding the walls of the sac with the attached overlying skin. The flaps thus formed are sutured to the bottom of the cavity, so that no dead spaces are left to suppurate or favor secondary complications. This operation is applicable to all aneurisms in which there is a distinct sac and in which the cardiac end of the main artery can be provisionally controlled. It is especially applicable to all forms of peripheral aneurisms of the larger arterial trunks, and, while the author has had no experience with similar lesions of the large visceral trunks, the principle suggested would appear to be applicable to abdominal, aortic, and other accessible forms of abdominal aneurisms. It is particularly indicated in the treatment of traumatic aneurisms in which the wounded artery communicates with a well-developed and circumscribed sac, and in all fusiform and sacculated aneurisms, whether traumatic or idiopathic, in which the conditions for securing provisional hæmostasis can be obtained. The method proposed does not contemplate the treatment of arteriovenous aneurism and the circumscribed or diffuse pulsating hæmatomas of recent origin which result from arterial and arteriovenous injuries. These cases offer admirable opportunities for the conservative application of arteriorrhaphy, with the view of preserving the lumen of the injured vessels and thus maintaining their functional value as blood carriers.

The steps of the operation as applied to peripheral aneurisms of the larger arteries are: (1) Prophylactic hæmostasis; (2) incision of the skin and exposure of the sac; (3) opening of the sac and evacuation of its contents, recognition of the type of sac, number of openings, etc.; (4) closure of the aneurismal orifice by chromicized catgut sutures; (5) removal of constrictor and test of sutures; (6) obliteration of the aneurismal sac.

The author has operated with success upon four cases by this method, two of which were direct traumatic aneurism of the brachial, caused by gunshot wounds, one of which involved the lower and the other the upper third of this artery, one femoral and one popliteal, and both of the so-called spontaneous variety. In conclusion the author submits the following propositions: (1) That the recognized advantages of the radical operation for the cure of aneurisms of the peripheral arteries, as demonstrated by the statistics of the last decade, can be greatly increased and the sphere of application of this operation can be broadened by the adoption of the method of suture and obliteration of the sac instead of the classical ligation of the arteries with or without extirpation, as hitherto practised. (2) That the closure of the arterial orifices which supply the aneurismal sac, whether these be single or multiple, by means of suture and within the aneurismal sac itself, greatly simplifies the technique of the radical operation, and is a reliable means of securing hæmostasis. (3) That in favorable cases—and the sacular aneurisms with a single orifice communicating with the lumen of the larger arterial trunks are the most favorable—it is possible by careful suture to obliterate the aneurismal opening without obstructing the lumen of the parent artery, thus protecting the limb from the risk of gangrene. (4) It is also possible in favorable cases of fusiform aneurisms of traumatic origin, and in those in which the sac material is healthy and pliable, to restore the lost continuity of the artery by building a new channel which will connect the two main orifices of communication and restore the interrupted circulation in the parent vessel. This result can be obtained by utilizing the sac in the manner previously described by the author. (5) That the fear that atheroma and other degenerative changes will interfere with the healing and repair of the arterial tunics has been greatly exaggerated is shown by the abundant experience of the aseptic period in the ligature of sclerotic arteries in continuity, in the absence of secondary hemorrhage in the amputated stumps of the aged, diabetic, and other arterially diseased subjects (Heidenhain, Webber, Barwell and others), and is still demonstrated more fully by the observations and statistics of the partisans of the radical operations by extirpation (Delbet, Kubler, Ransohoff, Annandale and others), who have reported numerous successful results in spontaneous as well as in traumatic aneurisms. (6) The fallacy and dangers of the old operation of Antyllus lie (*a*) in the fact that he preliminary ligation of the main artery above and below the sac will not always control the bleeding from the collaterals which often open into the aneurism or into the main trunks between the orifices in the sac and at the seat of ligature. This compels a more or less extensive dissection of the sac out of its bed as one of the necessary features of the procedure in order to secure all the collateral vessels that empty into the sac, unless the uncertain process of plugging the openings and packing the sac itself is resorted to. If the sac is dissected, as is usually done to secure the collaterals, the diffi-

culties of the operation are increased and the vitality of the limb is endangered by interfering with the collateral circulation which, in many types of aneurism, is most freely developed in the neighborhood of the sac. (*b*) Another serious objection to the old Antyllian operation as usually performed is that the sac is allowed to remain as an open cavity in the bottom of the wound, where it is packed or drained and allowed to heal by granulation. This invites infection, suppuration, and its attendant dangers of secondary hemorrhage; all that is obviated by the author's method of endo-aneurismorrhaphy, which does not disturb the sac from its vascular connections, and favors its prompt obliteration by insuring the infolded walls of the sac and keeping them in direct and close approximation. (7) The uncertainties and dangers of extirpation of the sac (Purmann's operation) are even more apparent than those of the Antyllus operation, because, in addition to the greater technical difficulties of extirpation, there is much greater risk of injury to the accompanying satellite veins and nerves which blend most intimately with the sac and often compel the operator to limit his intervention to a partial extirpation, leaving behind a considerable portion of the sac wall in order to avoid injury to important adherent structures. The greatest objection to extirpation, however, lies in the decided interference with the collateral circulation in the immediate vicinity of the aneurism, which entails a considerable risk of mortification in the distal parts. All these dangers are reduced to a safe minimum and are largely eliminated by simply obliterating the sac instead of extirpating it.

Remarks on a Second Series of Fifty Cases of Recurrent Appendicitis Treated by Operation.—Southam (*British Medical Journal*, January 10, 1903) states that this second series consists of 50 cases, of which 39 were males and 11 were females, the ages varying between ten and fifty-three years. In 5 cases there had been only one distinct attack, in 10 cases there had been two well-marked attacks, and in the remaining 35 cases three or more attacks. In almost every case the lumen of the appendix was either partially or completely occluded at some point in its course; sometimes close to its origin from the cæcum, sometimes at its middle or distal third. Though in most cases the walls were thickened, in a few, where the appendix was distended with fluid, they were extremely thinned. In one case, where the distention was extreme and the fluid contents were clear and watery, the appendix was quite translucent. It was frequently kinked or bent on itself at a right angle, and fixed in this position by adhesions which were present in the majority of cases, often firmer and more extensive after a few than after numerous attacks. In 3 of the cases collections of pus were found shut off in the distal portion of the appendix, which was dilated into a small cyst. In 6 cases there were fecal concretions, while in the remaining cases the contents consisted of a mucoid or mucopurulent fluid, which was sometimes mixed with fecal matter. In no case was any foreign body found. In 11 cases a localized suppuration had taken place outside the appendix, generally associated with a perforation of its wall. In 2 cases the patients had previously been operated on for appendicular abscess, and had had a recurrence of suppuration. These two cases illustrate the advisability of removing the appendix in all instances of suppuration—in recurrent as well as in first attacks—if this can

be effected without risk of breaking down the protective barrier of adhesions which shut off the collection of pus from the general peritoneal cavity. It is interesting to note that in many instances where marked lesions were found in the appendix there had been an absence of any local signs or symptoms during the quiescent periods between the attacks. Every case made a successful recovery from the operation.

Chloride of Ethyl in General Anæsthesia.—GIRARD (*Revue de Chir.*, November 10, 1902), after reviewing the subject in detail, states in conclusion: (1) General anæsthesia may be perfectly and completely obtained in man as well as in animals by chloride of ethyl. (2) Its action is rapid, it causes but slight excitement, and its application is made without resistance on the part of the patient, who awakes almost instantaneously after the withdrawal of the anæsthetic. (3) The rapidity of recovery demands that a close watch be kept by the anæsthetizer, and renders difficult a prolonged anæsthesia. (4) At the beginning of the anæsthesia it is important that the access of air to the respiratory tract be reduced to a minimum, and so a choice should be made of a good apparatus for inhalation. (5) The absence of nausea or vomiting after the cessation of anæsthesia makes this method the one to be preferred for all minor operations. (6) There is no need to fear any early accidents, for the absence of any irritant action upon the mucous membrane precludes any danger of reflex laryngitis. (7) However, it is necessary to watch for renal, hepatic, and cardiac lesions, as has been shown by pathological anatomy. This point should be cleared up before this method is generally used. (8) The mixed method seems to give the best results—shortening the pre-anæsthetic period, diminishing the amount of chloroform or ether required, suppressing of excitement at the beginning of anæsthesia and nausea or vomiting at the end; it possesses undeniable advantages and a certain superiority over simple anæsthesia. (9) The deaths which have been observed in animals after the anæsthesia has been established make it necessary to formulate certain reservations, for possible sudden depression of the respiratory centre may occur during the course of the anæsthesia (late syncope).

Surgical Intervention for Intestinal Perforation in the Course of a Case of Typhoid Fever; Recovery.—DEPAGE (*Jour. de Chir. et Annales de la Soc. Belge de Chir.*, November and December, 1902) states that this operation rests on a legitimate basis, as the statistics gathered by Boinet and Delenglade show that without operation 95 per cent. die, and that with operation the mortality varies between 79 and 88 per cent. Platt has collected from literature 103 cases of intervention, with 16 recoveries. The author's case was a woman of forty-two years of age, who presented the typical symptoms of perforation, and was operated upon three days after the perforation had occurred. A median incision under cocaine was made, and a collection of fetid pus was found on the side of the cæcum. Further exploration showed a small perforation in the small intestine about ten centimetres from the cæcum. A V-shaped resection of this portion of the intestine was then performed, the ends being joined in the usual manner. The intestines were then punctured with a small needle, so as to relieve them of a large accumulation

of gas, after which they were washed with hot sublimate solution, the focus of pus thoroughly washed out, and the abdominal wound closed, except at its inferior end, which was left open for drainage. The patient made an uninterrupted recovery. In conclusion the author states that an analysis of this case shows: (1) That perforation occurred at the twelfth or fifteenth day of the fever—that is to say, toward the end of the second week. (2) That the patient was not operated upon until three days after the perforation had occurred—that is to say, at the moment when the infection was general. The result in this case shows that even when the case seems perfectly hopeless it is, nevertheless, the duty of the surgeon to operate.

Note on the Value of Roux's Operation for the Radical Cure of Femoral Hernia.—Renton (*British Medical Journal*, December 27, 1902) states that he has found this method satisfactory in the ten cases in which it was used. It consists in (1) making an incision over the crural canal; (2) isolation of the sac, putting a catgut ligature around its neck, and cutting it off; (3) a metal staple is passed obliquely through Poupart's ligament over the crural canal, taking care to avoid the femoral vein, and then it is gently hammered into the pubis; (4) stitching the skin incision. The author states that care must be taken not to put the staple in too tightly, which would injure Poupart's ligament; still, it must be sufficiently secured to prevent any recurrence of the hernia. The staple remains permanently in situ; it causes no irritation, and does not injure the bone. Roux has reported over sixty cases in which the retention of the staple has given rise to absolutely no trouble, and there has been no recurrence of the hernia.

THERAPEUTICS.

UNDER THE CHARGE OF

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Toxicology of Adrenalin.—Dr. Taramasio reports on the toxic doses of adrenalin for frogs, guinea-pigs, and rabbits. Adrenalin was first prepared in 1901 by Takamine, following closely on Abel's work on epinephrin. It is a staple yellow powder, slightly soluble in water, and easily soluble in water of alcohol if acidulated with acetic or hydrochloric acid, and is considered to be by Takamine a basic salt with formula $C_{10}H_{15}NO_3$, but by Aldrich is thought to be $C_9H_{13}NO_3$. This drug gives a green color with ferric chloride, and a standard dilution of adrenalin has been fixed at that strength which

produces with a 15 per cent. solution of ferric chloride a green color only deep enough to last a few seconds, 1 c.c. of adrenalin solution so diluted, being called a ferric chloride unit. Thus one centigramme of the salt giving 700–750 ferric chloride units means that one centigramme dissolved in about 750 c.c. of water gives, with ferric chloride, a green tint which persists for ten seconds. Other preparations from suprarenal glands brought forward in previous years are: 1. Suprarenin, a red brown powder, which is a ferric compound introduced by Furth. 2. Epinephrin of Abel and Crawford, a benzol compound. 3. Sphygmogenine, a syrupy body, chemically indefinite, brought forward by Frankel. The second part of this report is taken up with the work of other men on the same subject. Many different animals have been used for experiment, but owing to different circumstances and the use of different preparations of the capsules it was impossible to gauge the dose of active substance which has toxic effects in each case. The author notes that Gourfein has said the toxic dose is very inconstant, but he finds but little variation in the fatal dose. In a general way, the results already arrived at are, that the blood pressure is greatly raised, the pulse is slowed, and respiration becomes more rapid and superficial. Pellicani is cited as the first to study the toxic action of suprarenal extract, thus finding that preparations from calves, oxen, and lambs are less toxic than those from carnivorous and smaller herbivorous animals; Oliver and Schäfer, as having rightly determined that vasoconstriction is due to a direct action on the smaller vessels, and is not of nervous origin, death being due, they considered, to bulbar paralysis, the respiratory centre being especially affected, and Cybulski (1896) as having brought forward pulmonary congestion as the direct cause of death. Finally, the work of Taramasio himself is given. He injected adrenalin dissolved in slightly acidulated water subcutaneously in the case of guinea-pigs and rabbits, and into the dorsal lymph sac in frogs. The following figures represent the dose of adrenalin injected per kilogramme of weight of the animal used for experiment:

	Dose never fatal.	Dose sometimes fatal.	Dose always fatal.
Frogs,	0.824 gram.	0.025 gram.	0.50 gram.
Guinea-pigs,	0.002 "	0.004 "	0.02 "
Rabbits,	0.002 "	0.004 "	0.01 "

Symptoms: dyspnœa, paresis with anæsthesia, and mydriasis in frogs appear a few minutes to an hour after injection, recovery, when it occurs, being complete within one, or at most, two days. Only six of the frogs treated with possible fatal doses died, though surroundings were unfavorable, the fact that pulmonary respiration is not necessary probably accounting for this slight toxicity, the skin taking on part of the functions of the lungs. Small doses cause slight increase of respiration in guinea-pigs, together with a slight fall of temperature, the prominence of the symptoms increasing in proportion to the dose. Sensation and motor power diminishing, death occurs generally within half an hour, and recovery, when occurring, being complete within a day. A blood-stained froth comes from the mouth and nose in the death agony, the heart continuing to beat after respiration has ceased. The lungs are found congested and covered with widespread ecchymoses, and acute œdema is the cause of death without doubt. The action of the drug

on rabbits, he states, closely resembles that on guinea-pigs; subcutaneous injection in both causing a slight slough, with a resulting scar, which is probably due to local anæmia, caused by contraction of the muscle walls of small arteries, for the anæmia itself prevents a rapid absorption from the point of injection. The author agrees with those who think pulmonary œdema causes death rather than with those who consider it a result of paralysis of the nervous system, though the latter action may be present to some degree in mammals, it plays a minor part. In frogs, on the other hand, the paralysis of the nervous system is thought to be the cause.—*Revue medicale de la Suisse Romande*, 1902, vol. xxii. p. 589.

Anæsthesin.—Dr. Chevalier reports on a new product, first discovered by Ritsert in 1890, but abandoned by him until recently, when Van Noorden, Dunbar, Lengemann and others have used it extensively, with excellent results. It is an ethylic ether of paramidobenzoic acid, and exists as a white powder without taste or odor; soluble with difficulty in 800 parts of water, but freely soluble in alcohol, ether, chloroform, acetone, fats, and oils. It is particularly adaptable in fatty combinations. Its dangers, if any, are due to its property of causing fixation of oxygen and the formation of methæmoglobinuria; but this takes place, according to Binz, in enormous doses only. Therapeutically it has been used with good results in ulcer of the stomach, gastric hyperæsthesia, in doses of thirty grains daily. In gastric irritability, doses of three to four grains prove efficient. In hyperæsthesia of the larynx it is used to advantage as a spray or as an inhalant, a 10 per cent. solution being used, oily or alcoholic. As a suppository in three to five-grain doses it is efficient in hemorrhoids. In a 10 per cent. lanoline ointment it has proven of inestimable service in a diabetic. Anæsthesin hydrochlorate may be employed hypodermically in 4 per cent. solution as an efficient local analgesic. Toxic or irritating effects have not been described.—*Revue de Therapeutique*, 1902, vol. lxix. p. 834.

The Active Principles of Rhubarb.—Drs. A. Tschirch and Henberger have restudied the question of the composition of rhubarb. Among the active principles they distinguish two groups of glycosides, tannoglycosides derived from rheotannic acid and anthraglycosides or anthracene glycosides. These pre-exist in the plant and are accompanied by a number of diverse products difficult to separate. The tannoglycosides are formed by the action of a left rotary sugar and of tannin (rhubarb red). The anthraglycosides are formed of the right rotary sugar and of different derivations of anthracene. Among these they mention chrysophanic acid, dioxymethylanthraquinone and trioxymethylanthraquinone, emodine, and rheine, which Tschirch thinks is a methyl ether of a tetramethylanthraquinone. All of these bodies are purgative.—*Pharmaceutische Zeitung*, 1902, vol. xviii. p. 547.

Treatment of Sydenham's Chorea by Arsenic.—Dr. P. Timacheff has made a careful analysis of arsenical therapy in twenty-six cases of chorea treated by arsenic in different combinations. In eight cases he used Fowler's solution, in six, Levico (an arsenical) water, in twelve he used an aqueous solution of arsenous acid after Comby's method. He preferred the last, both

from the standpoint of length of time of treatment and from the facility of administration. Among the many advantages of Comby's method of treatment there were also disadvantages. The most marked of these were the gastric and intestinal disturbances, nausea, and vomiting that were always present, and in rare instances diarrhœa follows. This nausea and vomiting was always the result of the ingestion of large doses of arsenic, and diminished on the withdrawal of the arsenic. The author's procedure was to give (1) as an initial dose one-half teaspoonful of the 10 per cent. solution, (2) increasing this half a teaspoonful a day (3) until a maximum dose of three to five teaspoonfuls a day was reached, (4) to continue this dosage for three to five days, according to the condition of the disease. Among the by-effects he noted herpes zoster in one, erythematous eruptions in two cases, and pruritus in one. Muscular soreness, paralysis, and paresis were not observed. As for recurrences, no arsenical therapy could prevent such.—*Medicinskore Obosrenie*, 1902, vol. xiv. p. 167 *et seq.*

Guaiacol Valerianate in Phthisis.—Dr. Kuhn administers this compound in doses of three to six grains in capsules or in drops with tincture of gentian. Stomachic disturbances may arise from the use of the gentian. In twenty instances ten showed marked improvement of appetite, in four there was a distinct lessening of the night sweats, in eight expectoration was diminished, twelve put on flesh. Tuberculous diarrhœa was not affected. The author concludes that combination possesses undeniable tonic properties, and is indicated in mild tuberculosis, in chronic bronchitis, and in bronchial dilatation.—*Therapeutische Monatshefte*, 1902, vol. xvi. p. 567.

PEDIATRICS.

UNDER THE CHARGE OF

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Tuberculous Meningitis, with Abnormal Onset.—E. Schlesinger (*Archiv f. Kinderheilkunde*, 1902, Bd. xxxiv., S. 355) reports a case under this title. The patient was a little girl, aged two and a-half years, whose brother had died a year before from tuberculous meningitis. The parents seemed to be in good health. The child, who had been in previous good health, suddenly became unconscious and developed violent convulsions, localized on the right side of the body, and affecting also the right side of the face. This condition, during which t he temperature rose to $101\frac{3}{10}^{\circ}$, lasted for five hours. The convulsions then ceased, and were replaced by a hemiplegia of the right side, complicated by aphasia, and accompanied by dimi-

nution of cutaneous sensibility and exaggeration of the tendinous reflexes of the same side.

On the third day the palsy had completely disappeared, and, aside from anorexia, with slight elevation of temperature, the child seemed in her usual health. But some days later the temperature rose and remained between $100\frac{4}{5}°$ and 102°, while gradually the classic symptoms of tuberculous meningitis appeared (vomiting, convulsions, rigidity of the neck, stupor), and death occurred fifteen days after the onset of the first symptoms.

A Case of Cured Tuberculous Meningitis.—K. BARTH (*Münchener medicinische Wochenschrift*, 1902, No. 21, p. 877) adds another case to the few recorded instances of cure of proven tuberculous meningitis. The patient was a girl, aged thirty-two months, who, following an attack of measles, was seized with vomiting, accompanied by headache and high temperature. On the fourteenth day of illness the author observed dilatation of the pupils, which reacted sluggishly to light, slight stupor, pronounced rigidity of the neck, and the presence of Kernig's sign, but the scaphoid appearance of the abdomen was not present. The other organs were not affected, the urine contained neither sugar nor albumin.

With the diagnosis of meningitis, iodide of potassium was prescribed internally, with ice to the neck and head, and baths with cold affusions to the head. The fever was not characteristic. Headache became more and more intense, the pulse slow, and the respiration assumed a Cheyne-Stokes type. Later appeared tonic convulsions of the upper and lower extremities, with opisthotonos and incontinence of urine and feces. The cerebro-spinal fluid showed the presence of tubercle bacilli.

The author then decided to try bloodletting, and applied wet cups to the mastoid regions. Under the influence of this intervention the temperature fell and the headache ceased completely. Little by little the symptoms of meningitis disappeared; but for sometime deafness and psychic blindness remained, with extreme weakness of the lower extremities—symptoms which finally yielded to appropriate treatment. The duration of the illness was about six months.

[It is to be hoped that the further progress of this case will be reported after the lapse of a year or more.—ED.]

Rubella Scarlatinosa.—Under this caption FREDERICK C. CURTIS and HENRY L. K. SHAW (*The Medical News*, December 20, 1902) report an extensive outbreak of an eruptive disease in the village of Round Lake, Saratoga County, N. Y., beginning early in April, 1901, in the family of a farmer who supplied milk to the residents of the town. Three children were slightly ill, with a temperature of about 100° F., and with pulse from 80 to 90. The throats were congested in all three cases, and the glands of the neck were enlarged; there was an eruption extending uniformly over the chest, trunk, arms, and legs, bright red, and strikingly suggestive of scarlet fever. Two of the children had had undoubted scarlet fever a few years before. Nineteen days after his visit to these children a young man on a neighboring farm was taken ill with well-marked rubella, while his sister, twelve years old, exhibited a rash on the chest and back identical with that of the cases

in the first family. The face of the latter was clear, and while the throat was sore, the temperature was only 99⅖°, and the child did not feel ill. On the following day the first case appeared in the village, and next day six cases developed, and the disease spread with great rapidity. One hundred and forty-seven cases were seen, and others were known to exist.

When the disease appeared in the village the diagnosis of scarlet fever, which had been made in the first cases, was questioned, and Dr. Curtis, one of the authors, was called in consultation. The endemic character of the disease was very striking. No attempt was made to quarantine the individual patients or the town, yet only a few isolated cases developed in the nearby towns. In the opinion of the resident health officer there seems to be some ground for believing that the infection was carried in milk. The first cases appeared in the family of the man who supplied milk to the village, and all the cases, with a few exceptions, occurred in families thus supplied. No instance of a nursing baby having the disease was observed, and two or three infants fed on cow's milk from another farm were not infected. A majority of the patients were adults, fully 60 per cent.

The evidence presented in a study of this epidemic warrants the conclusion that it was rubella, largely of the scarlatinal form. The diagnosis from mild scarlet fever was quite sharply drawn. In conclusion, the authors deprecate the recognition of the "fourth disease" of Dukes, believing that everything that has been said by Dukes in describing the fourth disease can with equal truth be stated in regard to rubella.

The Bacteriology of Empyema in Children.—W. J. S. Bythell (*The Medical Chronicle*, Nov., 1902, p. 81) presents a study of forty consecutive cases of empyema, the object of which was to determine not only the species of bacteria present, together with their source and path of infection, but also the part played by the bacteriology in influencing the clinical course and termination of the disease.

While common in children of all ages (ten months to eleven years), fully twice as many boys as girls were affected. The pleura is infected in the great majority of cases by a process of direct invasion from a pulmonary lesion, which in children is usually a catarrhal pneumonia. In many cases which are apparently primary the source of infection is probably also an undiscovered patch of bronchopneumonia. The micro-organism by far most frequently present is the pneumococcus, which occurred in pure culture in 26 out of 40 cases. The streptococcus alone occurred in two cases, while one or other of these organisms was present in every case except one, in which was found Friedlander's bacillus and the staphylococcus albus.

The clinical results of empyema depend to some extent upon the species of bacteria found within the pleura, the pneumococcic cases being, on the whole, the mildest. This micro-organism may, however, give rise to very serious complications, either by direct invasion of surrounding viscera or by metastatic infection.

The bacteriological examination of the pus gives other indications as to the clinical prognosis which appear to be of considerable value: (*a*) A small number of poorly-stained micro-organisms which give feeble cultures usually denotes a good prognosis; (*b*) the reverse condition is not so frequently ac-

companied by severe clinical symptoms, especially when phagocytosis is well marked; (*c*) vigorous cultures are not in themselves a reliable sign of pathogenic activity.

The bronchial glands are probably invaded by micro-organisms from the pleural cavity in every case. The organisms are sometimes also found after death in the mesenteric glands.

With the exception of those cases in which there are tuberculous lesions of the pleura or lung, the best results may be expected from the resection of a rib with free drainage. In cases in which a tuberculous origin is suspected, removal of the fluid by paracentesis is to be preferred, and especially when the lungs are the seat of tuberculosis. Free drainage in these cases probably offers no better chance of cure than repeated aspiration, and the complete evacuation of the fluid by free drainage appears to accelerate the pulmonary lesion by removing the pressure upon the lung, while the prolonged use of a drainage greatly increases the danger of contamination from without.

Infantile Scorbutus and Sterilized Milk.—Recent communications to the Paris Société de Pédiatrie by MM. Thiercelin and Guinon, reporting cases of infantile scurvy in infants fed upon sterilized milk, have brought out a paper from NETTER (*Revue Mensuelle des Maladies de l'Enfance*, December, 1902, p. 543), who claims to have called attention to this point in etiology in November, 1898.

Since that time numerous observers have reported similar cases. In the collective investigation of the American Pediatric Society, published in 1898, in which 379 cases of scurvy were tabulated, 84 occurred in infants fed exclusively upon sterilized or pasteurized milk. In the same year von Starck published 67cases, collected in Schleswig-Holstein, of which 18 at least were due to sterilized milk. In the present paper the author tabulates 23 observations from French sources, of which nine followed the use of milk sterilized at home or at the dairy.

Admitting that fresh milk is possessed of antiscorbutic properties, and that under the influence of heat this quality is destroyed, the author reasons that, while we do not know all the elements to which fresh milk owes these properties, we do know at least one which is diminished in sterilized milk, and this is precisely the substance which is par excellence the preventive against scurvy—citric acid, the active principle of lemon juice. Various investigators have shown the presence in fresh milk of an important quantity of citric acid in the form of calcium citrate. Henkel states that cow's milk contains from 0.9 to 1.01 grammes of citric acid to the litre, and Göldner has shown that this acid is combined largely with calcium and, in very small proportions, with potassium and magnesium. Others have found this acid in the milk of other animals. Scheibe estimates the proportion per litre in human milk at 0.5 gramme, and in the milk of the goat at 1.5 grammes. According to Vaudin, this citric acid plays an important rôle in keeping the earthy phosphates in solution. In a word, as Corbette puts it, a litre of milk contains as much citric acid as an ordinary lemon. Corbette has also shown that the amorphous tribasic citrate of fresh milk is much more soluble when cold than when hot, and that under the influence of prolonged boiling it is transformed into the much less soluble crystalline citrate, which is precipi-

tated in large part and is only partially dissolved in cooling. The transformation and consequent loss of citric acid in solution will therefore be the more complete as sterilization is prolonged, as the cooling is less rapid, as the absence of subsequent agitation does not permit the redissolution of a part of the precipitated crystals. It seems certain that the milk of the cow normally holds a proportion of citric acid greater than the needs of the infant, since it is double that of human milk. It is therefore evident that even after sterilization cow's milk may preserve sufficient of its soluble citrates to prevent the development of scurvy, and that many infants may be fed upon sterilized milk, especially in the lesser dilutions, without developing scorbutic symptoms. But it is impossible to be assured that at any moment this balance may not be disturbed, owing to natural diminution in these antiscorbutics in the milk itself, or to greater prolongation of the sterilizing process. An observation of Medin's in 1898 at the children's hospital in Stockholm is very suggestive in this connection. Medin observed within a few months 15 cases of infantile scurvy in infants fed upon milk sterilized in the hospital by means of the Soxhlet apparatus, while in the preceding ten years not a case had been observed among the infants fed upon milk sterilized by the same method.

Attention is also called to the fact that milk is frequently subjected, not once but several times, to repeated cooking or sterilization. Neumann, in Berlin, in 1901 and 1902, collected a considerable number of cases of scurvy among families making use of a milk from an excellent dairy. It was found that, as a further precaution against contamination of the milk, the whole output of the dairy was regularly pasteurized before delivery to its consumers. As a result of Neumann's investigation, this dairy issued a circular to its patrons advising against further sterilization of the milk in the household, or that, at least, the time of ebullition in the sterilizer be reduced to one or two minutes at the most.

A later communication of von Starck (*Verhandlungen der Gesellschaft deutscher Naturforscher*, Hamburg, 1901) showed that infantile scurvy had become much rarer in Schleswig-Holstein since these facts had been recognized. Three years after his first investigation, in which 67 cases had been collected, a second inquiry among 300 physicians of the country obtained only 22 cases, 5 of which had been fed on maternized milk, 4 on sterilized milk (Soxhlet), 1 on sterilized milk, 2 on boiled milk, 2 on milk and barley soup, 4 on barley soup exclusively, and 2 on oatmeal soup.

While insisting upon the significance of citric acid contained normally in milk, and its diminution under the effect of heat, Netter is not convinced that the antiscorbutic properties of fresh milk are contained exclusively in its citrates. There are other antiscorbutic elements which are modified by heat or other agents, and it is extremely probable that they exist in milk.

In the infrequent cases of scurvy in infants nourished at the breast, the author believes that the mother's milk, under peculiar conditions, has lost to some considerable degree its antiscorbutic properties. Ill-health of the mother resulting from wasting disease, or other cause, such as prolonged mercurial treatment, may thus act in rendering her milk very poor in its antiscorbutic elements. In the case reported by Crandall in 1899 the mother had heart disease, with marked anæmia, and had been confined to bed since the baby's birth.

OBSTETRICS.

UNDER THE CHARGE OF

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The Efficiency of Disinfection of the Hands by Hot Water and Alcohol.—AHLFELD (*Monatsschrift für Geburtshülfe und Gynäkologie*, 1902, Band xvi. Heft 5) has long believed that the hands can be safely disinfected by the use of hot water and alcohol. He mentions a striking illustration, as follows:

He had occasion to induce labor in a patient with contracted pelvis, who had lost children by embryotomy. The case proved to be an obstinate one, and the child perished during the labor. The mother was taken with violent chills, followed by high temperature, and it was necessary to deliver the child by embryotomy. Although the head was opened the child failed to descend, and accordingly the abdomen was opened, the uterus incised, and the child delivered by Cæsarean section.

Great care was taken to disinfect the hands thoroughly with hot water and alcohol, and at the time when the uterus was opened basins containing hot water and alcohol were placed conveniently for the operator, and the hands were frequently rinsed in these fluids. Cultures from the body of the child revealed the presence of abundant staphylococci. The mother made an uninterrupted recovery, her temperature rapidly falling.

The alcohol employed was 96 per cent. in strength.

Two Cases of Pregnancy and Labor Complicated by Atresia and Stenosis of the Vagina.—KERMAUNER (*Monatsschrift für Geburtshülfe und Gynäkologie*, 1902, Band xvi., Heft 5) reports the case of a patient in her first labor, who had a protracted parturition, ending in the delivery of a dead child with forceps. A week after her confinement she had incontinence of urine, and examination showed a vesicovaginal fistula. The loss in substance was so great that extensive operation was necessary to restore the wall of the bladder. This reduced the size of the vagina very greatly. She came under observation when the second time pregnant.

On examination she was found to have a considerably contracted pelvis; the entrance to the vagina was much altered in size and shape, while the vulva had been practically closed by the preceding operation. When the patient came into labor she was delivered by Cæsarean section, with amputation of the uterus and extraperitoneal treatment of the stump. She made a good recovery, her child surviving.

The second case was that of a patient who, after her first confinement, lasting three days, recovered, with incontinence of urine and septic infection. A large vesicovaginal fistula had been repaired after her first labor.

She also had a considerably contracted pelvis, the external antero-posterior diameter being 17.5 centimetres.

On examination a double promontory was found with a true conjugate of 8.5 centimetres. The transverse diameters of the pelvis were normal. On examination the induction of labor was declined because it was thought that the head could pass through the pelvis, and it was believed that the scar tissue present would dilate at labor. It was thought best to allow the patient to come into labor spontaneously, and then, should the necessity arise, to perform Cæsarean section.

When labor occurred the head entered the pelvic brim transversely. An effort to dilate the scar tissue in the vagina by a Barnes bag failed, and Walcher's position was necessary to secure the insertion of the bag. Multiple incisions were made in the cervix to loosen the scar tissue, and a solution of cocaine was applied. Suppositories of opium were given, and the character of the pains became much better. The head gradually descended, the scar tissue was stretched, and under strong pressure upon the abdomen the head was born spontaneously. The child was slightly asphyxiated, but quickly revived and survived. There was no laceration found upon examination. The mother made an uninterrupted recovery.

The second case illustrates the extraordinary possibilities of spontaneous parturition. It must be observed, however, that this patient was in a hospital where interference could be undertaken at any time, and that every essential help was given to her labor by the use of drugs and by incisions in the cervix. It is evident that had the patient received no help her child must have perished, and quite possibly the mother also.

The Most Efficient Preparation of Ergot.—PALM (*Monatsschrift für Geburtshülfe und Gynäkologie*, 1902, Band xvi., Heft 5) analyzes the effect produced by different preparations of ergot, and has made personal observations and experiments to determine which of these is most advantageous. He believes that the efficient principle of ergot is largely chrysotoxin, and that sphacelotoxin is most advantageous of all these preparations. In subcutaneous administration the dose is from $\frac{1}{100}$ to $\frac{1}{10}$ of a drachm, which produces prompt uterine contractions. The remedy has little effect upon the general condition of the patient. Palm regards the hypodermic use of ergot as much superior to the administration of ordinary preparations by the mouth.

Cæsarean Section by Transverse Incision of the Fundus.—CURSCHMANN collected (*Monatsschrift für Geburtshülfe und Gynäkologie*, 1902, Band xvi., Heft 5) 119 cases of Cæsarean section by transverse incision of the fundus. He gives statistics to prove his belief that the transverse incision offers no essential advantage over the usual incision upon the anterior uterine wall. He supports his assertion by measurement of the uterine wall at the fundus, and, anteriorly, by a comparison of convalescence after the two methods and by minute study of the cases. The mortality was 12.1 per cent., or 13 cases, 11 of which were cases in which the uterus was retained, and 2 cases in which the uterus was removed. One patient was admitted to the hospital in a septic condition. The causes of death were as follows: Carcinoma of

the uterus, 1; purulent bronchitis, 1; embolism of the lung, 1; death from shock immediately after the operation, 1; peritonitis, 8. In 3 cases autopsy showed adhesions of coils of intestine with the uterine wound. This was also seen in several cases which recovered in which it was necessary to do abdominal section for the relief of obstruction of the intestine.

Repeated Cæsarean section was done in 10 cases, in 8 of which the first operation was made by longitudinal incision in the anterior uterine wall, while in two transverse incisions of the fundus had been practised. In all of these cases there was adhesion between the uterus and the abdominal wall and omentum. No scar in the uterus could be discovered in these cases. Of these 10 repeated sections, 7 recovered without fever, 1 had fever and recovered, and 1 died.

Hydatiform Mole, with the Report of 2 Cases and Collection of 210 Cases.—FINDLEY (*Medical News*, December 6, 1902) reports 2 cases of this condition and summarizes his study of the subject as follows:

The causation of hydatiform mole is unknown. It is most frequently found between the ages of twenty and thirty years, more often in multiparæ. It probably results from degeneration of the villi of the chorion through some disturbance of maternal circulation. The connective tissue stroma of the villi degenerates, with serous infiltration or œdema. The syncytium and Langhan's cells penetrate more deeply when maternal nutrition is defective. In 16 per cent. of cases malignant degeneration occurs. It is very difficult to draw the line between benign and malignant cases. The examination of a specimen gives but little information regarding it. Retention of a mole within the uterus does not influence its disposition to become malignant.

Diagnosis can only be positively made from seeing the vesicles. The most constant clinical point lies in the rapid development of the uterus, with irregular shape and consistency and hemorrhage.

The treatment of the condition consists in emptying the uterus at once. Because the womb is thin and weak it is best to avoid the use of the curette and to employ ergot and vaginal packs to control the hemorrhage and stimulate expulsion. After the mole is expelled, the uterus should be explored with the finger, irrigated and packed with iodoform gauze. Two weeks after the birth of the mole the uterus should be curetted, the scrapings examined, and if malignant disease is beginning, hysterectomy should be performed. The patient should be kept under observation for three years afterward, and should hemorrhage occur the uterus should be again curetted and the scrapings examined microscopically.

Statistics show the average age of these patients to be twenty-seven years, the extremes being thirteen and fifty-eight years. In one patient eleven moles developed. In 8 cases there was cystic degeneration of the ovaries. In 1 case the mole developed in the Fallopian tube. The longest period at which malignant disease occurred after the development of the mole was four and one-half years. The mortality of this condition is 25 per cent. The causes of death are: syncytioma malignum, 16 per cent.; hemorrhage, 4 per cent.; septic peritonitis, 2 per cent.; other causes making up the remainder.

GYNECOLOGY.

UNDER THE CHARGE OF

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Adenoma Malignum.—HERMANN (*Centralblatt für Gynäkologie*, 1903, No. 44) describes a case of cancer of the portio, which was admitted to Saenger's clinic as inoperable, the broad ligaments being involved. The treatment consisted in curettement and cauterization with chloride of zinc, which relieved the patient for six months, when it was necessary to repeat the operation on account of recurrence. She was relieved for another period of six months, when the same treatment was adopted. A profuse serous discharge persisted, but there was no return of the hemorrhages, which were profuse before the first curettement. Microscopic examination of the growth last removed showed an ordinary glandular formation of a benign type, offering a marked contrast to the malignant course of the disease.

The writer infers that the growth was a true malignant adenoma. Of the nineteen cases of malignant adenoma reported in the literature, seven were really adenocarcinoma. In the case reported the relatively benign character of the growth was shown by the fact that it had existed for seven years, yet the patient remained in good health. He suggests that the profuse mucous discharge, which never became purulent, may be regarded as an important point in the differential diagnosis between malignant adenoma and adenocarcinoma.

Vaginofixation and Ventrofixation.—DIRMOSER (*Centralblatt für Gynäkologie*, 1903, No. 44) reports sixty-nine cases of vaginofixation from Erlach's clinic in Vienna, in the majority of which Dührssen's method was adopted. Forty-one patients who were kept under observation were cured. Of the forty-nine cases of Dührssen's operation, one patient became pregnant and had a normal delivery. Of the seventeen in whom the round ligaments were shortened per vaginam, seven were subsequently delivered one or more times, and one aborted.

Ventrofixation was performed seventy-six times, fifty-eight patients being kept under observation. Four patients were delivered at term and two aborted.

Benign Epithelial Proliferation in the Corpus Uteri.—HENGGE (*Centralblatt für Gynäkologie*, 1903, No. 44) reports two cases of uterine hemorrhage in patients, aged forty-four and forty-nine years, in which tissue removed with the curette showed under the microscope circumscribed and diffuse epithelial growths, without loss of substance. In one case there was accom-

panying glandular hyperplasia. Pregnancy, cancer, and tuberculosis were positively excluded. There was also no evidence of an inflammatory process. No cause for the peculiar epithelial proliferation could be discovered; in fact, the writer regards these cases as unique.

Leucocytosis in Pelvic Suppuration.—Dützmann (*Centralblatt für Gynäkologie*, 1903, No. 47) reports 165 cases in which he was enabled to establish the presence of pus in the pelvis before operation. Pus was never found when the blood count was normal. The writer was even able to infer the cause of the suppuration from the number of leucocytes, a count of 20,000 to 30,000 pointing to streptococcus infection, while one of from 11,000 to 13,000 was commonly associated with the presence of gonococci or colon bacilli. In peritonitis and septic infection an increase in the leucocytes is a favorable sign, even in the presence of persistent elevation of temperature. If, on the contrary, there is no increase while the temperature is high, a fatal termination may be expected; this is probably due to deficient phagocytosis.

Alcohol as a Disinfectant.—Schaeffer (*Centralblatt für Gynäkologie*, 1903, No. 47) believes that it is impossible to render the hands sterile by any method of disinfection. After repeated experiments, he finds that by scrubbing for five or ten minutes with green soap and for five minutes with absolute alcohol the best results are obtained. It is, however, necessary to change the alcohol after each washing. Moreover, the germ-destroying action of the alcohol is lost in a few minutes if the hands are immersed in watery fluids, blood, or serum.

The principal value of alcohol, in the writer's opinion, is its power of removing fat and epithelium—that is, its mechanical purifying action.

Vaginal Hysterectomy.—Nigrisoli (*Centralblatt für Gynäkologie*, 1903, No. 46) reports 462 vaginal hysterectomies with 11 deaths (2.38 per cent.). Of these, 55 operations were performed for cancer, with 4 deaths; 14 abdominal hysterectomies were done for cancer with 2 deaths. The writer now prefers the abdominal route in all cases, except when the uterus is prolapsed and the disease is absolutely limited to the organ. Seven patients, operated upon before 1898 and 5 since then, were still without recurrence.

There were 56 vaginal hysterectomies for fibromyoma, with 1 death, and 98 abdominal, with 8 deaths; 41 cases of ectopic gestation (25 operated upon per vaginam) were all successful; 274 radical vaginal operations for diseased adnexa were followed by a mortality of 5, and 300 abdominal resulted in 18 deaths. Only 1 fatal case is noted in 168 vaginal sections for the evacuation of pus; in 75 abdominal sections for the same condition there were 10 deaths. In 34 conservative vaginal sections there was no mortality.

The writer used the angiotribe in 50 cases, but always employed ligatures in addition.

Vaginal Ovariotomy.—Heinsius (*Centralblatt für Gynäkologie*, 1903, No. 46) reports 700 cases of colpotomy in the Greifswald clinic during the last three and one-half years. Of these, in 110 oöphorectomy was performed,

the anterior incision being preferred, as it is believed that the parts are rendered more accessible. Five deaths resulted, 3 due to the escape of pus, and 2 to improper catgut. Martin's mortality in 262 vaginal cœliotomies was only 3 per cent.

The writer believes that this is the ideal method of removing small tumors which are not adherent above the true pelvis. Cystic tumors as large as a man's head can be removed in this way, but it is not advisable to attempt the removal of solid growths larger than the fist.

Ovarian Parotitis.—Troitzky (*Ronsk. Wratch; La Gynécologie*, 1902, No. 5) reports a peculiar epidemic of mumps in a boarding-school, in which one-third of the patients complained of pain in the ovaries as well as in the parotids. When only one parotid was affected the ovary in the corresponding side was tender; both ovaries were attacked simultaneously with both parotids. The ovarian pain and tenderness developed after the parotid swelling and diminished progressively with the latter. In girls who menstruated no menstrual or mammary disturbance was noted. The writer infers that although oöphoritis is a rare complication of mumps as compared with orchitis, it is doubtless more common than is usually supposed, being overlooked on account of the situation of the ovary and the difficulty of examining it.

The exact nature of the anatomical changes is not positively known, but it may be inferred that there is either a perioöphoritis or a parenchymatous inflammation analogous to that observed in other infectious febrile diseases. It usually occurs in girls above ten years of age. The possibility of this complication of mumps should always be borne in mind, and if ovarian symptoms appear suitable treatment should be instituted.

Radical Operation for Cancer of the Uterus.—Kleinhans (*Centralblatt für Gynäkologie*, 1903, No. 43) reports thirty-two cases of radical abdominal hysterectomy, with three deaths. He curettes and cauterizes freely and clamps off the vagina before opening the abdomen. In cases of cancer of the cervical canal he prefers amputation. All glands which can be felt are removed, since, according to different observers, from 27 to 57 per cent. are cancerous. The writer believes, with Rosthow, that the glands are early involved. It is often very difficult to determine before operation whether indurations of the broad ligaments are inflammatory or malignant. Sometimes an exploratory laparotomy is necessary in order to determine this point.

Cancer of the Uterus.—Pozzi (*La Gynécologie*, 1902, No. 5) concludes his paper read before the International Medical Congress with the following deductions: 1. The surgical treatment of uterine cancer rarely insures relief extending beyond two years. 2. Hysterectomy is not justifiable if the uterus is fixed by indurations in the surrounding tissues. 3. The importance of infection of the lymph nodes has been exaggerated, since recurrence usually takes place in the cicatrix; hence extirpation of the glands, even when it is supposed to be complete, seems to have little influence on the return of the disease. 4. Abdominal hysterectomy is a more

serious operation than vaginal, on account of the greater risks of infection, and should be reserved for special cases in which the vagina is narrow, the uterine wall softened, or the cul-de-sac extensively involved; also, when the uterus is unusually large or complications are present—fibroids, pregnancy, pyometra, or pyosalpinx. In a few instances the abdominal route may be preferable, in order to dissect out the uterus from the diseased tissues. 5. Vaginal hysterectomy is accordingly preferable on account of the smaller risk, the ease with which it may be performed in the early stage of the disease, and the fact that even a palliative operation is preferable to a "pseudocurative" one in which the chances of an immediately fatal result are so great.

DISEASES OF THE LARYNX AND CONTIGUOUS STRUCTURES.

UNDER THE CHARGE OF

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Sarcoma of Branchial Cleft.—Dr. James E. Newcomb, of New York, reports this case (*Medical News*, October 26, 1901), which occurred in a man, aged sixty-five years. Two years previously he noticed a swelling on the right side of the palate, with a soreness in the gums adjacent. The swelling gradually increased for a year when it was lanced, giving escape to thin, clear fluid, with permanent subsidence of the pain. Lancing had to be repeated several times on account of recurrent swelling. The growth was removed by Dr. Weir through an external incision. A bluish, cystic tumor, reaching upward almost to the base of the skull, was carefully shelled out. It was about the size of a mandarin orange, on one side of which was a solid mass, in size and shape resembling a tonsil. The report of the examination at the laboratory of the Columbia University Medical School read: "Telangiectatic sarcoma of the branchial cleft, with hyaline degeneration; lymph nodes hyperplastic; no tonsillar tissue."

True Papilloma of the Nasal Septum.—Dr. James E. Newcomb, of New York, reports (*Ibid.*) a case of true papilloma of the left side of the septum in a man, aged fifty-five years. The case had been sent to him on account of severe epistaxis, which was found to be due to a large erosion on the convex of the septum, which was strongly bulged to the right. Some bibliographic references accompany the report.

Morbid Growths of the Nose: Osteosarcoma of the Inferior Turbinate.—Dr. James E. Newcomb, of New York, reports (*Medical News*, October 26, 1901) a case in a colored male subject, aged forty-one years, who had had an increasing obstruction in the right nasal passage for some four

months, but without pain or hemorrhage. A bony adhesion was found between the inferior turbinate and the septum, which was removed with the trephine. Recurrence ensuing a few weeks later, the core of tissue was removed with the trephine and found by Dr. Jonathan Wright to be an osteosarcoma. Further treatment was not allowed.

Angiofibroma of the Nose.—This case was reported by Dr. Newcomb (*Ibid.*), which occurred in an Irish-American, aged twenty years, who for seven months had complained of alternating nasal obstruction, finally becoming permanent, on the left side. Inspection revealed an apparent polyp hanging from the middle turbinate, but posterior rhinoscopy disclosed a mass in the rhinopharynx, apparently blocking the left side only. The anterior growth was so hard that it resisted the cold wire snare, bleeding freely. A small portion removed with considerable hemorrhage, which was checked with difficulty, was found microscopically to be an angiomatous fibroma. Its point of origin could not be determined, and the patient refused further surgical interference.

Nasal Polypi the Cause of Atrophy of the Optic Nerves.—At a recent meeting of the French Society of Ophthalmology (*Archives de Médécine et de Chirurgie Speciales*, May, 1902), Dr. Parisotti reported a case of a young man, aged twenty-five years, whose vision rapidly diminished to 1/50 on the right and 1/10 on the left, the papillæ becoming pale and almost on the point of being completely blanched. Rhinoscopic examination was at first negative, but subsequently revealed hypertrophy of the turbinates, and polypoid vegetations of the middle meatus. After the ablation of these growths vision increased progressively, so that five months later it equalled I in both eyes, the papillæ remaining very white. Six months later, however, vision had receded to 4/10. The author attributes these optic troubles to a spasmodic ischæmia produced by the nasal vegetations.

Foreign Body in the Larynx.—Dr. Oliver A. Blumenthal, of Syracuse, N. Y., reports (*American Medicine*, August 30, 1902) a case of a triangular fragment of bone one and one-half inches long impacted in the larynx; the sharp-pointed end was in the left arytenoepiglottic fold and the broad end in the right fold. The bone was released and extracted with laryngeal forceps under guidance by the laryngoscopic mirror.

Morbid Growths of the Larynx.—Dr. Joseph D. Bryant, of New York, reports (*Journal of the American Medical Association*, October 18, 1902) an interesting case in a patient, aged forty-five years, of a large tumor of the posterior wall of the larynx low down, removed by enucleation after external access by low lateral pharyngotomy. It weighed 425 grains, and was $1\frac{7}{8} \times 1\frac{3}{4} \times 1\frac{1}{2}$ inches in its antero-posterior, vertical, and transverse diameters, respectively. Muscular fibres were found in the structure, leading to the surmise that it must have originated in muscular tissue. The lateral pharyngotomy was selected because digital exploration had revealed an apparent attachment of the tumor to the right portion of the pharyngeal wall. When exposed to digital exploration through the external wound,

the growth was found quite immovable and apparently firmly attached to the posterior wall of the pharynx. The finger, introduced through an incision between the tumor and the mucous membrane covering it, completely enucleated the growth, leaving its entire membranous envelope intact. The patient made a good recovery. A number of somewhat similar instances were reported by gentlemen who took part in the discussion of this paper before the Section on Surgery and Anatomy of the American Medical Association at its fifty-third annual meeting.

Foreign Bodies in the Air Passages; Escape of the Outer Tube of a Durham Tracheal Canula.—Dr. E. D. Ferguson, of Troy, N. Y., reports (*New York State Journal of Medicine*, October, 1902) the escape into the right bronchus of the outer tube of a Durham double canula in consequence of the neglect of the manufacturer to provide it with the necessary protective flange at its outer extremity. Its removal was effected by incising the tracheal wall down toward the bifurcation, when, with the finger, the missing tube was felt in the right bronchus, the upper extremity being well within the bronchus. With the aid of illumination from a head mirror the upper edge of the tube was seen, and it was removed with forceps.

PATHOLOGY AND BACTERIOLOGY.

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Multiple Progressive Hyaloserositis (*Studies from the Royal Victoria Hospital*, Montreal, vol. i., No. 3).—Under the foregoing title Nichols discusses the etiology, morbid anatomy, and clinical aspects of that form of a chronic proliferative process affecting serous surfaces "characterized by the formation of a membrane composed of dense layers of connective tissue of a peculiar cartilaginous appearance." This membrane, which may be several centimetres in thickness, is a continuous stratified layer, and can be peeled off from the subjacent affected organs. The upper part of the peritoneum, particularly the liver and spleen capsules, the bases of the pleural cavities, and the pericardium are the parts oftenest involved. As a result, the structures attacked may show atrophic, degenerative, or even fibroid changes.

As a localized liver lesion the process has been described as chronic hyperplastic perihepatitis, chronic deforming perihepatitis, and by Curschmann as

the "zuckerguss" or iced liver, from the porcelain-like or "frosted" appearance. Though the liver may be primarily and solely involved, the process is usually progressive, affecting the serous surfaces consecutively, but all may not show the peculiar "icing" appearance. The main theories as to the causation of the process are pericarditic pseudocirrhosis (Pick), chronic nephritis (Hale White), and inflammation (Curschmann).

From a careful study of his own and thirteen reported cases of "zuckerguss" liver, Nichols would prove that the first two hypotheses are incorrect. Reasoning from the clinical and pathological evidences at hand, he concludes that the etiological factor is a chronic inflammatory process caused by some micro-organism of slight virulence. The tubercle bacillus is capable of producing quite similar but still distinct lesions.

The pathological findings make clear many of the clinical manifestations. Ascites is constant; anasarca and emaciation are common. The great omentum is often contracted and indurated. The liver, which is usually almost completely invested by the frosted membrane, is generally small and deformed, with round edges and a smooth surface. In the great majority of cases there is no cirrhosis; there are, however, fatty and parenchymatous changes and passive congestion. The gall-bladder is frequently involved in the perihepatitis. The right pleural cavity is more frequently seriously involved than the left. This is strikingly more common at the base of the right lung, the central tendon of the diaphragm, and the right side of the pericardium. Chronic adhesive pericarditis is usually present; the pulmonary and cardiac changes are what would be expected under the conditions. The spleen, which is commonly enlarged, is often frosted, particularly when there is left-sided pleural involvement. It may be atrophic in advanced cases. No special abnormality appears in the kidneys. An acute terminal infection of many of the serous sacs or of the lungs is frequent.

Histologically, this "icing" is found to be a laminated fibrous tissue, with more or less hyaline transformation and giving evidence of being an organized inflammatory exudate.

Clinically, only the cases with the frosted liver are found to admit of diagnosis, and the symptoms vary considerably according as the liver is primarily or secondarily affected.

The average age of onset is about thirty years; the duration varies from two to sixteen years, averaging six years. The sexes appear to be about equally affected. The onset may be either acute or very insidious. The primary infection is most frequently in the pericardium, next in or about the liver, and less often some other peritoneal inflammation. Alcohol, gout, and syphilis appear to have little and heredity absolutely no etiological significance. The constant and striking physical sign is the extreme ascites requiring repeated paracentesis. The ascitic fluid is straw-colored, of a specific gravity of less than 1010, but twice as rich in albumin as a transudate, which is cited as evidence of its inflammatory causation.

If the process is primarily pericarditic anasarca appears first, then a train of symptoms following the extension of the inflammatory process to the liver *via* the right pleural cavity, and finally the ascites. If the liver is primarily involved there is epigastric pain, sense of fulness in the abdomen, and dyspnœa, followed by a slowly developing ascites, and then perhaps an ex-

tension to the right pleura and pericardium, with consequent clinical signs and symptoms. Icterus is not present in uncomplicated cases. The urine is decreased in amount, and albumin is commonly absent. The prognosis is eventually hopeless. The treatment is purely symptomatic. Unusual precaution should be taken against exposure to acute infections.—J. L. Y.

The Intestinal Origin of the So-called "Fever of Infancy" (Fiebre de Borras).—DUENAS (*Revista medica Cubana*, January, 1903, No. 1) suggests the possible relation of this Cuban infantile fever with the summer diarrhœa of infants of the United States. The recent work of Duval and Bassett has shown that at least certain forms of summer diarrhœa of children are due to the bacillus dysenteriæ of Shiga, as shown by the presence of this organism in the stools of such cases and the agglutination reactions on the organism with the blood of those ill of or convalescent from the disease.

In a case of the author's, a girl of twenty months, who had been suffering for several days with persistent bloody vomiting, pain in the epigastrium, and mucus and ill-smelling stools, a distinct fever and rapid pulse, the patient's blood twenty days after the beginning of the disease gave a positive reaction with the bacillus dysenteriæ in dilutions of 1:60. This case the author further regards as significant of the possible relation of this bacillus with certain of the "black vomits" attended with fever and of unknown etiology.—F. P. G.

The Inheritance and Intra-uterine Transmission of the Agglutinating Properties of the Blood and the Formation of Agglutinins in the Bodies of Embryos.—JUREWITSCH (*Cent. f. Bac. u. Para.*, 1902, Bd. xxxiii. p. 76) states that the agglutinating properties of the blood of normal pregnant rabbits and guinea-pigs for typhoid bacilli was first determined. The blood of some normal rabbits possessed this power in 1:80 dilutions. The blood of the young from such mothers also had the power to agglutinate typhoid bacilli, but in less degree than the mothers. Occasionally in a litter from a single mother certain animals showed agglutinins in their blood, while others did not. With normal guinea-pigs neither the blood of mothers nor young showed any tendency to agglutinate typhoid bacilli. Normal pregnant guinea-pigs were now immunized against typhoid bacilli during the time of pregnancy, so that at the birth of the young agglutination took place with the mother's blood in 1:4000 or 1:5000 dilutions. In three out of thirty-one cases no agglutination could be demonstrated in the young. In all the other cases agglutination was obtained with the blood of the young, but was three to thirty times weaker than with the blood of the mothers, and after a short period the blood of the young lost this property entirely. In order to determine whether the agglutinins were simply transmitted through the placenta to the blood of the young, or whether the fœtus was actually endowed with the power of producing agglutinins, the mothers were subjected to a passive immunity, and agglutinating sera from previously immunized guinea-pigs, rabbits, and horses were injected into the pregnant mothers. After a few hours Cæsarean section was performed and the blood of the young tested. The result was the same as when the mothers were immunized during pregnancy. It was further found that the blood of young normal rabbits coming from a

normal mother whose blood agglutinated typhoid bacilli did not lose their agglutinating properties as they grew older, but, on the other hand, showed in some instances agglutination in higher dilutions than the mother's blood. The author believes these animals inherit the power of producing agglutinins. Guinea-pigs which had previously been immunized were allowed to become pregnant. The young of these animals showed the power of agglutinating typhoid bacilli often in much higher dilutions than the mothers.—W. T. L.

A Contribution to the Knowledge of the Pathological Changes Following Thyroid Extirpation in Rabbits.—Bensen (*Virch. Arch.*, 1902, Bd. clxx. p. 229) states that the experiments may be divided into three groups: First, rabbits from which the thyroids had not been removed were fed upon thyroid extract; second, the thyroid gland was removed and no thyroid extract given; and, third, the thyroid gland was removed and animals then fed upon thyroid extract. In each series of experiments the animals were killed after a certain number of days and the thoracic and abdominal organs examined. In the first group the animals were killed after receiving 0.3 grain of thyroid extract twice daily for twenty-four days. Sections of the liver showed fatty infiltration and hyperæmia. Colloid droplets were found in the convoluted tubules of the kidney. The pathological changes were, however, not very marked in any organ. In the second group of experiments extensive degenerative changes were found in the kidneys, liver, and heart muscle. In animals that lived thirty to forty days after the operation the kidney tubules were filled with enormous amounts of colloid, sometimes appearing in long cylinders, and if life was prolonged from 100 to 150 days there was, besides the presence of colloid, such an extreme grade of degeneration of the kidney epithelium that even the nuclei were much affected. The liver and heart muscle showed the same general type of extreme cellular degeneration. In those animals living longest proliferative changes were noted in the kidney and liver. Infiltration of leucocytes sometimes occurred in the liver. The splenic changes consisted principally in hyperæmia and pigmentation. No alterations were observed in the stomach, pancreas, parotid gland, tongue, adrenal, and generative organs. In the third group of experiments changes similar to those first described were found, but in much less degree. The author concludes that when the thyroid glands of rabbits are extirpated a poison is either produced or withheld in the body which gives rise to a peculiar degeneration of the cells of the kidney, liver, and heart muscle. The product of this cell degeneration appears as colloid droplets or in the kidney tubules even as long colloid cylinders.—W. T. L.

The Relations Between the Lymphatics and the Connective Tissue.—W. G. MacCallum (*Johns Hopkins Hospital Bulletin*, 1903, vol. xiv. p. 1) says: By means of silver staining, v. Recklinghausen, in 1862, showed that the walls of the lymphatic capillaries are composed of a single definite layer of flat polygonal endothelial cells. He supposed, however, that the walls were incomplete and that the lymphatics were in direct communication with the intercellular spaces of the surrounding tissues. Hiss, Teichmann and others opposed the idea of the lymph canaliculi, and believed in the integrity of the lymph vessels. MacCallum has studied by means of injections, and silver stains the lymphatics of the skin of embryo pigs. In sections

stained with hæmatoxylin and eosin the lymphatics could be readily made out as vessels wide in comparison to the capillaries, and lined by a single layer of cells with clear protoplasm and flattened-out nuclei. A fine black line surrounded each of these cells in silver stains. Clear spaces were seen in the surrounding tissue, and often lay next to the clear endothelial cells of the lymph capillaries. The resulting appearance was that of an apparent opening in the wall of the lymphatics. That this was not actually the case could be shown in silver stains, followed by a nuclear stain where the intercellular spaces stained black and surrounded the clear spaces, each one of which proved to be a clear cell with central nucleus. These cells were branching, and without the nuclear stain suggested anastomosing channels. When the lymphatics were injected with silver solution the lymphatic vessels stood out in sections as a network of smooth-walled vessels, with a quite perfect lining of tessellated endothelial cells, and the intervening and surrounding tissue was not stained. From these observations the author concludes that the lymph canaliculi or "saft kanälchen" of Recklinghausen cannot be injected or in any other way demonstrated to be in connection with the lymphatics, but are cells whose outlines are stained with silver nitrate. When the lymphatics were injected with methylene blue, small extravasations of the blue fluid occurred along the course of the vessel if much force was used. Under the microscope these extravasations took place in a sudden explosive manner, and when pressure was made upon the specimen the lymphatics were emptied, but the extravasations were left unchanged. The process of development of the lymphatics appeared analogous to that of the bloodvessels. Sprouts of single cells or of several cells projected from the lymph vessels, and sometimes bridges of cells connected two vessels. The lumen was apparently formed by separation of parallel cells or from the hollowing out of a single cell. Experiments to determine the manner of transporting foreign granules showed that the process was carried on, as far as could be determined, entirely by phagocytic cells. Injections of granular material were made into the subcutaneous tissues of rabbits, and in sections made several days later through the lymphatic trunks relatively little free pigment was found. Almost all the granules were inclosed in cells.—W. T. L.

HYGIENE AND PUBLIC HEALTH.

UNDER THE CHARGE OF

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AND

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Ptomaine Poisoning.—From time to time cases of several members of a family, or a number of families suffering from acute poisoning after eating tinned meats, frozen rabbits, etc., are reported in the public press, and

within the last few months they have been of rather frequent occurrence; but none has surpassed in severity and extent one in which nearly two hundred persons in widely distant parts of the country were attacked with pains, purging, and vomiting, with alarming prostration, and in several cases a fatal termination, after partaking of pork pies bought at or about the same time from one of the best shops in Derby. The manufacture of pork pies is the staple industry of Melton Mowbray, in Leicestershire, and these enjoy a European reputation; but those of many other makers in the north midlands are in no way inferior, and among them those of the firm in question stand deservedly high. There was nothing in the taste or appearance of the pies to arouse suspicion, but Professor Délépine found a bacillus resembling the B. enteritidis of Gaertner—in fact, that known as the B. Friedebergensis of Gaffky—and succeeded in extracting from the jelly a toxin fatal to guinea-pigs and rabbits. In this instance the poisonous character was common to the whole of the pies or to a large number of them, made at the same time, and must therefore be ascribed to the condition of the carcasses or to some unknown accident incident to the preparation of the pies in general, whereas it is more often peculiar to one among many.

Probably the most remarkable example of ptomaine poisoning was one reported in 1892 by the late Dr. E. Gwynn, Medical Officer of Health of Hampstead, and absolutely unique in its virulence. The food in this instance was one of the well-known Paysandu tongues, which a gentleman, his wife, and two children were about to partake of for breakfast. On opening the tin they remarked its somewhat dry appearance and the absence of jelly. He, noticing something unpleasant in the smell, forbade them to eat it, and proceeded to divide an omelette among them, using for this purpose the same fork. The wife and elder child, who had just tasted but had not swallowed the tongue, were seized about noon with symptoms closely simulating those of Asiatic cholera—pain, vomiting, involuntary watery evacuations, and collapse—the mother being for some hours cold, pulseless, and unconscious. The father and the other child, who had not tasted the tongue, and had merely eaten the omelette touched with the infected fork, were attacked in the afternoon with vomiting and faintness, and the child sank into a profound stupor, from which she could not be aroused for some hours. They all ultimately recovered, but for some time the life of the lady had been almost despaired of. Mr. Stokes, the analyst, found parts of the tongue softened, acid, and charged with tin and iron dissolved by the acid. Professor Macfadyen obtained therefrom cultures of the usual bacteria of putrefaction. Mr. Stokes' assistant, who put into his mouth a piece the size of a shilling, "to see how it tasted," suffered from vomiting and giddiness for thirty hours. Mr. Wynter Blyth endeavored by Brieger's method to extract some alkaloids, but without success, and the results of injections of solutions of the extract on guinea-pigs were negative, from which he concluded that the poison was a toxalbumin or enzyme—bodies at once the most virulent and the most unstable, and which had disappeared in the interval of five days that had elapsed between the opening of the tin and his experiments. He expressed the opinion that the failure of the most careful investigations after inquests on undoubted cases of meat poisoning may be thus explained.

Scurvy: A Chronic Ptomaine Poisoning.—The etiology of scurvy had long been one of the most obscure and vexing problems in pathology; but the hypothesis put forward a few years ago by Professor Tomp, of the University of Christiana, and advocated by MR. KOETTLITZ, Medical Officer to the Jackson Harmsworth Arctic Expedition, in the *British Medical Journal*, February 8, 1902, offers the only rational explanation, reconciling and rendering intelligible many apparently conflicting facts and experiences. Tomp and Koettlitz maintain that scurvy is nothing more or less than a chronic poisoning by ptomaines formed by certain bacteria in imperfectly preserved foods. Other factors may conduce to the production of the disease, not, indeed, as efficient causes, but as predisposing conditions, especially by diminishing the power of resisting or of destroying the poisons; and the well-known, though not infallible, prophylactic action of lime juice may be due to its in some way neutralizing or antagonizing the toxins.

It is a fact that a continuous diet of salt beef or pickled pork, especially when these preserved meats have been kept for many months, is almost inevitably followed by the appearance of scurvy in a ship's crew, and that it never arises among those who enjoy a diet of fresh meat, vegetables, and fruit, and rarely when, in default of these, or when they can be supplied at intervals only, the diet consists of good tinned meats and vegetables, with the addition of sound dried fruits, vegetables, with potatoes and lime juice.

Other organic acids, even vinegar, are reputed to possess some antiscorbutic properties, and Dr. Neale, of the steamship Eira, claimed for draughts of fresh blood the exemption of the crew.

But in some Arctic expeditions in which the food was entirely or almost entirely preserved, but by the absolute exclusion of the air after complete sterilization, as those of Professor Nordenskjold and Dr. Nansen, not a trace of scurvy appeared in the course of three or four years. More striking still was the experience of the Jackson Harmsworth expedition. The exploring party, who partook at least once daily of fresh meat in the form of bear's flesh, enjoyed perfect health; while those who remained on board their ship, though taking their doses of lime juice every day, suffered without exception from scurvy, of whom two died. But it is to be remembered that they frequently remarked on the decidedly "high" or "gamey" taste and smell of the meat when the barrels were opened, and they could not be induced to eat fresh bear's flesh on account of its coarseness and peculiar flavor.

In fact, whatever else they had, the meat contained more or less of the ptomaines; while their comrades on land, though with less variety and without any lime juice or other reputed antiscorbutics, did not suffer from ptomaine poisoning, the flesh on which they mainly subsisted being perfectly fresh. So, too, Nansen and Johannsen did not suffer in the least during their sixteen months' solitary sojourn in Franz Joseph Land, though they had no vegetable food whatever, and, unlike the exploring party of Harmsworth's expedition, lived entirely on the flesh of the bears they killed; and we may assume that the crew of the Eira would have enjoyed no less freedom from scurvy without having had forced on them the repulsive draughts of raw blood. Nansen's crew, on the other hand, being for three

whole years, whether free or ice-bound, on the high seas, had no opportunity of obtaining fresh meat, but were entirely exempt from scurvy, thanks to the excellent preservation of their food.

Like Nansen himself and his companions, the members of Leigh Smith's expedition, twenty-five in number, who were wrecked on Franz Joseph's Land in 1881, and wintered there under the most miserable conditions, subsisting for a whole year on a diet exclusively of fresh and often raw flesh, maintained their health to the last.

The peasants in Russian Lapland, though able to obtain farinaceous, saccharine, and vegetable foods, suffer much from scurvy, for the fish which constitutes the nitrogenous part of their diet is generally more or less tainted, from imperfect preservation in winter and from an acquired preference for the taste of "high" fish in summer.

In short, the whole theory of the possession by any foods or drugs of antiscorbutic properties as such is a delusion. No food, if perfectly free from incipient putrefaction, whether it be fresh or preserved in an aseptic state, will cause scurvy; nor under such conditions will hardship, exposure to cold, depressing mental surroundings, or physical discomfort conduce thereto. On the other hand, incipient putrefaction, if it be so far advanced as to produce any change in the flesh perceptible to the taste or smell, will certainly—and even if it be not may sooner or later—give rise to that form of chronic ptomaine poisoning known as scurvy.

The etiology of infantile scurvy or scurvy rickets (Barlow's disease) is not touched on by Mr. Koettlitz, and does not at first sight seem to admit of so simple an explanation; but since it never occurs in infants at the breast, it is not unreasonable to assume that ptomaines of a kindred nature may be produced in artificial foods by the bacteria in the milk with which these foods are prepared.

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ANATOMICAL STUDY OF A SHORT-LIMBED DWARF, WITH SPECIAL REFERENCE TO OSTEOGENESIS IMPERFECTA AND CHONDRODYSTROPHIA FŒTALIS.[1]

By Ludvig Hektoen, M.D.,
of Chicago.

In the winter of 1901 there fell into my hands the body of one Thomas Wilson, concerning whom the following facts are all that are known at this time: He could not walk very well and supported himself by selling lead-pencils and chewing-gum from a roller chair. He was a hard drinker. Two persons who knew him during life state that in their opinion he was of ordinary intelligence. It is unfortunate that nothing is known of his early life. He died January 5, 1901, in a so-called "bum lodging-house," at the supposed age of forty-five years. A post-mortem examination was made by the physician to the coroner's office, and rupture of the gall-bladder is mentioned in the certificate as the chief cause of death. The body was then kept in a refrigerator until March 7, 1901, when a second post-mortem was made, with the following result:

There is a sutured post-mortem incision from the top of the sternum to the pubes, and there is also a sutured incision in the left arm. The body is diminutive in size; the head and trunk are more nearly normal in size; the lower extremities are perceptibly shorter in proportion. In the lower extremities, especially the legs, the skin seems to be looser than usual; there is a moderate curvature of the spine in the thoracic region, the convexity extending forward and to the left, with a marked curve in a forward direction in the lumbar region. The bones of the extremities are the only ones that show any abnormalities on external examination. The long bones are the seat of various curvatures and nodular enlargements, especially at the articular ends. In the left humerus there is a distinct interruption of the continuity in the lower third, but this has not the appearance of a recent fracture, and crepita-

[1] The skull is described by Charles A. Parker, M.D., and the thyroid examined chemically by H. G. Wells, M.D.

tion is not obtained. (In the X-ray photographs of the body, kindly made by Dr. Smith, resident physician of the Presbyterian Hospital, the bones of the skeleton are seen to be excessively porotic, anomalous in form, the long bones being greatly swollen at the ends.) The right knee-joint is larger than the left, and there is a swelling in the head of the right tibia, which crackles on pressure. Incision into the joint shows a soft mass from which red hemorrhagic material can be scooped out. There are no evidences of decomposition, but there is considerable drying up of the tips of the fingers and toes, and of the nose, lips, and penis; the latter seems to be very small. The nose appears rather thin and sharp, and the root does not seem to be any more deeply inserted than is ordinarily the case. There is no distinct depression at the root. Two small testicles are felt in the scrotum. Otherwise the external examination reveals no further morbid lesions.

The following measurements were made:

Length of body	95	cm.
Estimated weight	75	lbs.
Length of right upper extremity	48	cm.
" left " "	49	"
" hands	15	"
Breadth of hands	6	"
Circumference of middle of right arm	30	"
" " " left "	30	"
Length of right lower extremity	37	"
" left " "	36	"
" feet	13	"
Breadth of "	7	"
Vertical diameter of patella	3	"
Circumference of right knee	28	"
" of left knee	24	"
" of middle of right thigh	27	"
" of middle of left thigh	25	"
" of head	30	"
Distance from tip of chin to highest point of head	27	"
" " root of nose to chin	11	"
" " glabella to occipital protuberance	21	"
" " " to protuberance over top of head	35	"
" between zygomatic arches	12	"
" from meatus to meatus over top of head	36	"
" between malars	11	"
" " angles of lower jaw	8.5	"
" from tip of chin to pubes	42	"
Length of spine (sacrum 7, lumbar 12, thoracic 18, cervical 11)	48	"
Circumference of neck	26	"
" at shoulders	69	"
" of chest at nipples	69	"
" of abdomen at navel	57	"
" of pelvis at level of superior spine	57	"

The body cavities are found filled with sawdust soaked in formalin. The heart, lungs, spleen, pancreas, liver, kidneys and lower urinary organs, testicles, and organs of the neck do not present any gross lesions recognizable at this time. All the organs are smaller than those of a normally developed, full-grown man. The heart weighs 145 grammes; the kidneys, 105 grammes; the spleen, 30 grammes; and the thyroid, which is symmetrical and flattened, 9 grammes.

The diameter of the aorta at its beginning is 9 millimetres; in the middle of the descending portion it is 1 centimetre.

FIG. 1.



Photograph of the body. Note relative shortness of the limbs.

The gall-bladder does not show any changes, but there is a tear across the centre of the free aspect.

The bones of the skull are rather thin and cut easily with the saw. The brain is quite soft, and the hypophysis weighs 0.65 grammes.

The skeleton was prepared for articulation and mounting.

HISTOLOGICAL EXAMINATION.

Heart. There are no special changes. The number of nuclei in the muscle cells seems rather large. The striations are absent, the fibres are narrow, and branch and anastomose unusually freely.

Thyroid. In some parts of the gland there is no evidence of thyroid structure present—the gland here appears to have been entirely replaced by fibrous and muscular tissue. For the most part the typical follicular structure is replaced by fibrous tissue with oblong and variously-shaped spaces filled with rather small cells of various shapes, the nucleus staining diffusely, the cell body being without any distinct wall (Fig. 3), the nuclei are relatively large, the surrounding finely granular cytoplasm staining a light pink with eosin. In no place do these cells assume a distinct cuboidal form, and, as stated, there is no trace of any follicular arrangement. Small masses of homogeneous or finely granular colloid mate-

FIG. 2.

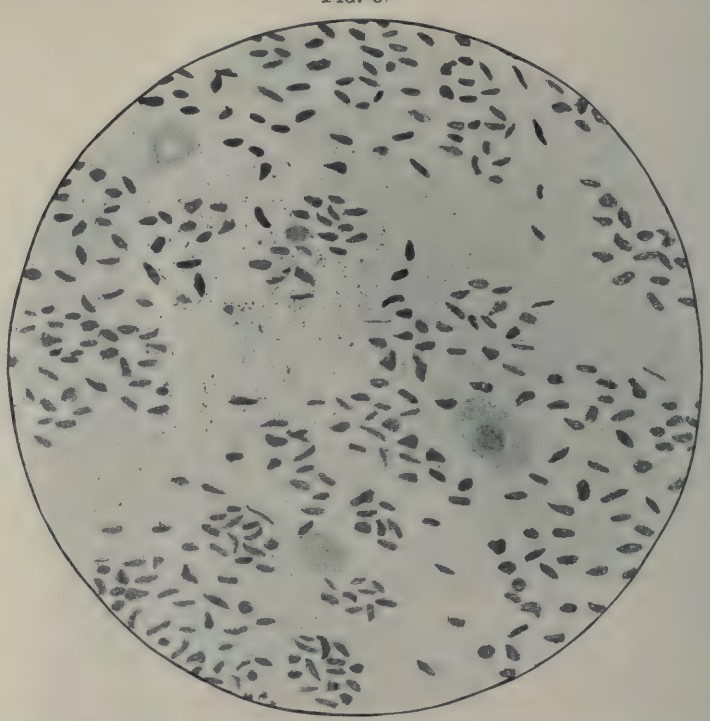


Photograph of the body.

rial occur here and there. Generally but one or two such masses appear in the field of a No. 3 objective. Sometimes colloid masses lie in spaces containing but few cells, the walls being formed by fibrous tissue. At other times the spaces are lined with endothelial cells. The thyroid contains a moderate number of bloodvessels of normal appearance; in some of the larger arteries at the margins there is fibrous proliferation in the intima and calcification of the elastica.

Hypophysis. The structure seems quite normal. There are small masses of colloid in a few of the follicles. There are no distinctly eosinophilic or cyanophilic cells present, the cell bodies generally assuming a light pink color in hæmatoxylin and eosin sections.

FIG. 3.



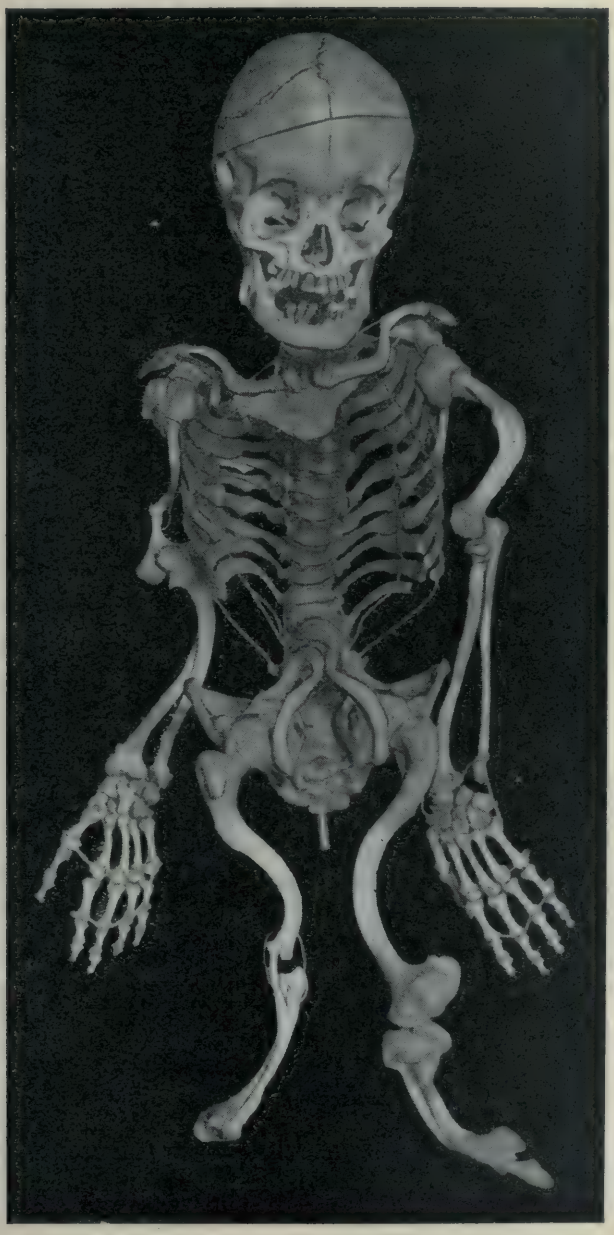
Fibrosis and atrophy of the thyroid, with occasional colloid remnants.

Bones. Sections of bony tissue from various bones, especially the upper end of the right tibia, show an exceedingly spongy structure; for the most part only isolated fragments of bone occur, hardly any complete Haversian systems being present; there is no evidence of excessive lacunar absorption or halisteresis, but the number of bone corpuscles seems larger than usual. The marrow is fatty.

CHEMICAL EXAMINATION OF THE THYROID (by Dr. H. G. Wells). The thyroid gland, except such part as had been used for histological examination, was received in alcohol. In order to avoid possible loss from solution in the alcohol the fluid was evaporated to dryness in the incubator and the residue added to the gland substance, which was similarly dried. The weight of the substance combined was 0.766 grammes. Analysis was performed in the same manner as in the series previously studied, that is, by the modified Baumann's method. The residue from the infusion, after being evaporated, was shaken with 10 c.c. of chloroform, and no coloration whatever was imparted

to it. Therefore, if any iodine at all was present it was but a minute quantity, not over 0.05 milligramme. The average amount of iodine per gramme of dried thyroid in residents of Chicago has been found to be about 2 milligrammes.[1]

FIG. 4.



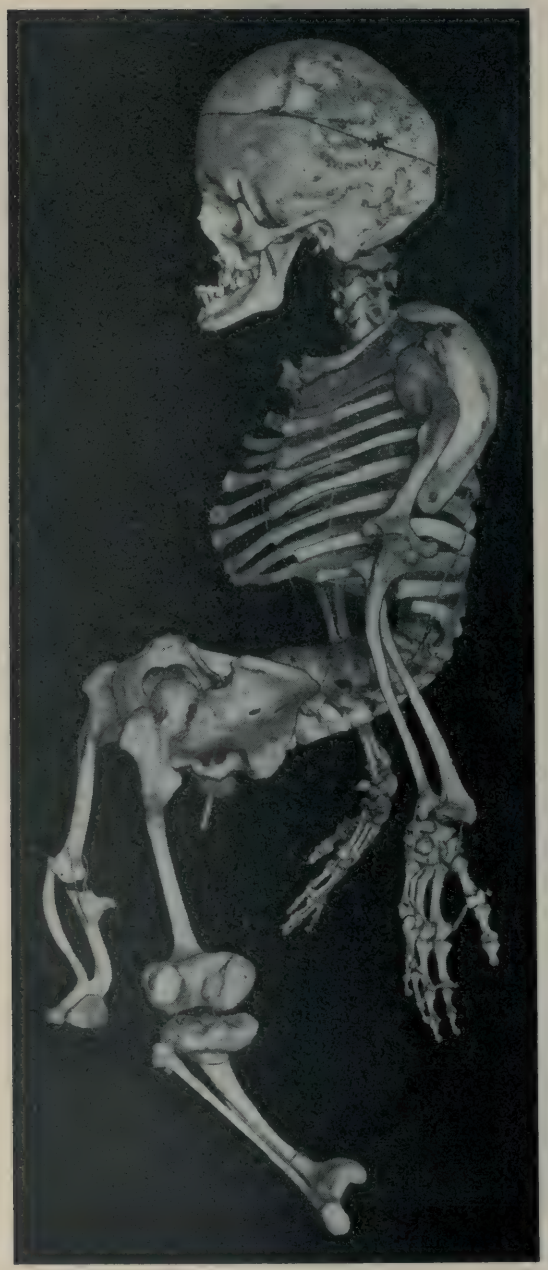
Photograph of skeleton. Relative length of upper extremities in this and in the two succeeding figures due to imperfect articulations, especially at the shoulder-joints.

EXAMINATION OF THE MOUNTED SKELETON (Figs. 4, 5, and 6). The skeleton as a whole is small and light, the total weight, including

[1] Concerning the method of analysis, see H. G. Wells, "The Physiology and Therapeutics of the Thyroid Gland and its Congeners." Journal of the American Medical Association, October 30, and November 6 and 13, 1897.

an iron rod to hold the spine together and copper wires at the majority of the joints, being only 1817 grammes. The bones in general are light and spongy; there is no sclerosis anywhere, the external as well as the internal architecture presenting many and striking variations

FIG. 5.



Photograph of skeleton. Left lateral view.

FIG. 6.



Photograph of skeleton. Right lateral view.

from the normal. The usual normal anatomical markings are greatly disturbed, often absent or not recognizable. In the following description only the essential and most remarkable departures from the normal type are mentioned briefly. The spine contains the usual

number of vertebræ. There is a slight curvature forward and to the left in the upper thoracic region, resulting in some elevation of the left shoulder. At the junction between the eleventh and twelfth thoracic vertebræ occurs a sharp bend forward almost to a right angle. The bodies of the twelfth thoracic and of the first lumbar vertebræ are much flattened, being 1 cm. in thickness in front. At the lumbosacral junction the sacrum bends backward nearly to right angles, but the lower end of the sacrum is bent forward at an acute angle, the coccyx projecting between the ischia.

The shoulder-blades are small and thin, and of a distinct fœtal character. In the right subscapular fossa is a defect 2 cm. in diameter, with smooth but thin margins. There are no distinct glenoid cavities, the enlarged heads of the humeri being partially received into a concavity formed by the elongated coracoid processes, which make a semicircle, and parts of the margins of which seem to form articular surfaces.

The normal curves of the clavicles are exaggerated. The right clavicle is 10 cm. long, the left 11.5 cm.

There is a slight thickening at the costo-chondral junctions. The heads and necks of the first five right ribs are more or less absorbed and amalgamated with the corresponding vertebræ by osseous tissue. The third, fourth, and fifth are broken at or near the angles; in the case of the third and fourth there seems to be false joints at the sites of the fractures; in the case of the fifth the fracture may be post-mortem. The vertebral ends of the first and second ribs are embedded in a rather irregular bony growth. There is an old ununited fracture, with smooth surfaces in the sixth right rib, about 6 cm. from the costo-transverse junction; another in the sixth left rib, about 3 cm. from the spine.

The humeri are misshapen, enlarged at the ends, and in the case of the right humerus, which is bent almost to a semicircle, the shaft is quite thick. The heads of the humeri are swollen into irregularly globular masses, 4.5 cm. in diameter, and composed of crumbling, spongy bone. At the junction of the lower and middle third there is a break in the left humerus; the ends are somewhat swollen and irregular; the opposing surfaces are fairly smooth; for some distance on each side the bone is thin and slender. The right humerus is 17 cm. long, the left 16 cm.

The bones of the forearm are more or less curved, especially those of the right forearm, but there is no marked enlargement of the articular ends. At the junction of the middle and lower third of the right radius is a fusiform swelling such as might be caused by the healing of fracture. The right ulna is 17.5 cm. long; the left 19 cm.; the right radius 17 cm.; the left 19.5 cm.

The bones of the carpi, the metacarpal bones, and the phalanges seem normal in shape and size.

The pelvis presents marked deformities (see Figs. 4, 5, and 6). The bones are thin, light, and fragile. The alæ, especially in the regions of the fossæ iliacæ, are quite like parchment, and there are two oval defects with thin but smooth margins in the left and one in the right, from 1 cm. to 1.5 cm. in diameter. At each acetabulum the bone seems to have been pushed toward the sacro-iliac articulation, so that the distance between the corpus ossis-ischii and the sacrum on the left side is less than 1 cm., and on the right side about 2 cm. There is no

distinct acetabular rim. The superior-posterior parts of the acetabular rims have large facets for articulation, with reciprocal surfaces on the anterior portion of the superior surfaces of the necks of the femurs. The foramina obturata face each other, the incisuræ acetabuli being very large, 3.5 cm. and 4 cm. in diameter. The pelvis is of an irregular hour-glass form. Diameters: At inlet—transverse, 10 cm.; antero-posterior, 4 cm.; oblique, 8 cm. Of cavity—transverse, 2.5 cm.; antero-posterior, 9 cm. At outlet—transverse, 6 cm.; antero-posterior, 6 cm.

The femurs are similar in general outline, both describing a large curve with the convexities toward each other. The lower ends are greatly expanded and contain large spaces; the lower end of the right femur has crumbled away considerably. The neck is short, relatively thick, the head large, exceedingly spongy. The right femur is 19 cm. long, the left 20.5 cm.

In the dry condition the left tibia and fibula measure 17 cm. in length. The ends are swollen, especially the upper end of the tibia, which is expanded more or less mushroom-like. Both bones are curved, the convexity being directed in the front. The upper ends of the right tibia and fibula have crumbled away. These bones are also curved extensively, and 3 cm. above the ankle the fibula is united to the tibia by a flattened bridge 1 cm. wide.

The bones of the feet are exceedingly light, consisting of a very thin compact layer, externally and interiorly, of larger and smaller cavities separated by walls of extreme thickness. Many of the smaller bones crumbled down, and it was not possible to articulate the feet.

The Skull (Dr. Charles A. Parker). The skull[1] presents on lateral view an unusually high cranium overtowering a small receding face and protruding lower jaw. In front it has a narrow oval outline with high orbits and irregular teeth.

The maximum length is 17.2 cm., the maximum breadth 13.2 cm., with a corresponding circumference of 49.5 cm. The height from the basion, or anterior margin of the foramen magnum to the bregma, inside measurement, is 15 cm. Although a comparison of these figures with those averaged from ten normal skulls shows both the breadth and length to be slightly over 1 cm. short of the average, yet the height, which is increased by 2 cm. (the compensation relation), completely compensates for the circumferential contraction, as shown by the capacity of 1450 c.c., that of the average normal male skull.

The cephalic index is 76.7, hence the skull is of the meso-cephalic type.

The internal surface of the base presents little variation from the average skull in form or measurements; the foramen magnum is normal in size, shape, and location, as are also neighboring parts of the occipital bone, except the upper part of the tabular portion, which is composed of Wormian bones.

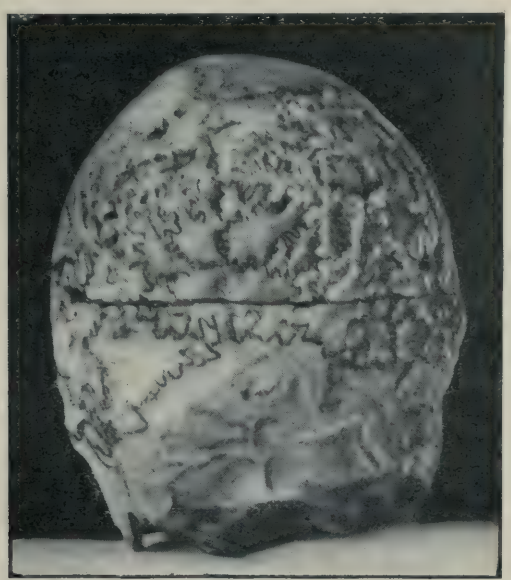
The thickness varies from 2 mm. laterally, in the temporal region, to 9 mm., in the frontal and occipital the average being 4 to 5 mm. The distance from the basion to the foramen cæcum is 1 cm. above the average, which, considering the shortness of the skull and normal

[1] Further consideration of the skull will be given by Dr. Parker in a separate article concerning Wormian bones.

location of the basion, appears disproportionate, but is explained by the absence of the frontal sinus and crest. The foramen is situated 1 to 2 cm. nearer the anterior surface of the skull and correspondingly farther from the basion. It is not unusual to find the distance from the glabella to the foramen over 2 cm., while in this skull it is less than 1 cm.

The distance from the basion to the occipito-sphenoidal synchondrosis is normal, as is also the distance from the latter to the anterior superior angle of the sphenoid at the cribriform suture. The cerebral surface of the presphenoid measures 2.5 cm., while the postsphenoid measures but 2 cm., giving an index of 125 obtained by dividing 100 times the former by the latter, the angle being very close to 100 or both parts equal. In a series of skulls examined the maximum was 113 and the minimum 87.

FIG. 7.



Photograph showing Wormian bones of cranial vault.

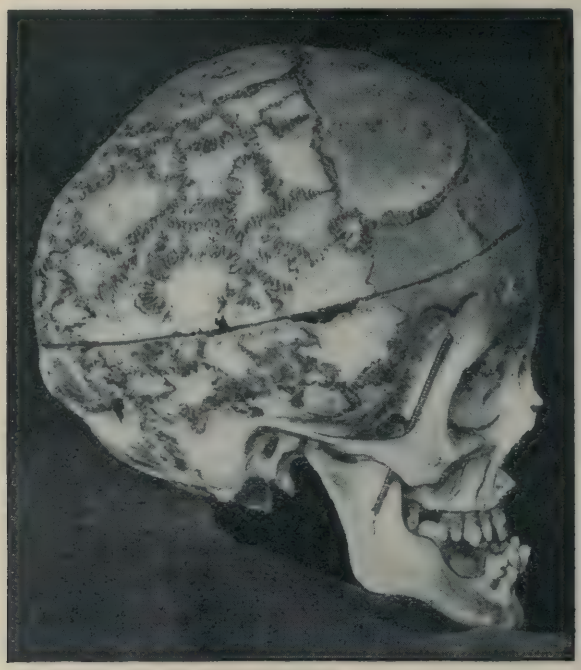
While the total length of the cerebral surface of the sphenoid is not affected, the disproportion between the two portions is unusual and constitutes the only noteworthy variation from the ordinary measurements of this region. Although somewhat asymmetrical in general outline, the entire cranium presents but slight variations from the normal measurements, the moderate circumferential constriction being accompanied by vertical elongation, with undiminished capacity, and the disproportion between the presphenoid and postsphenoid making no difference in the length of the floor.

The peculiar shape of the skull, with the recession of the face, may be represented by superimposing an outline of a median section of the skull upon a similar outline of an average normal skull, so that a line from the basion to the spheno-cribriform junction, the basal line of Huxley, is one exactly corresponding with a similar line in the other, their uppermost ends being at the same point (see Figs. 4 and 7).

Wormian Bones. The most striking feature of the skull is the extraordinary development and distribution of Wormian bones, numbering 172 (Figs. 7 and 8). They are most numerous in the posterior and lateral regions of the skull, supplanting the parietals, the squamous portions of the temporals, and the upper half of the tabular portion of the occipital. They are generally stellate in form, their numerous interlacing processes presenting an extensive pattern of delicate inlaid work. Several occur in the vertical and orbital portions of the frontal bones.

The inner surface is smooth, showing only the larger dentations, the finer process being limited principally to the outer layer. The parts free from them are the lower portion of the tabular plate, the condylar and basilar portions of the occipital, the mastoid and petrous portions of the temporals, the sphenoid and ethmoid bones, or those bones primarily developed in cartilage, the chondro-cranium.

FIG. 8.



Photograph showing Wormian bones of cranial vault.

The sagittal suture is distinct throughout, and extends from the nasion to the chondro skeleton of the squamo-occipitalis, separating the parietal bones and dividing the frontal and membranous skeleton of the squamo-occipitalis into lateral halves. The coronal suture is well marked and sharply limits the forward extension of the Wormian bones, though one in the vertical portion of the right frontal bone and some in its orbital plate are in front of it. The lambdoid and squamous sutures cannot be traced. The sutures at the base show no special variations.

The frontal bone, which is divided into two parts by the persistent sagittal suture (metopic), presents a very high vertical portion and small orbital plates. In the upper part of the right half, bordering on the coronal and sagittal sutures, is a large quadrilateral Wormian

bone measuring 5 cm. by 9 cm., separated from the rest of the bone by a horizontal suture. Twelve small Wormian bones are located in the suture between the orbital plates and the alæ parvæ of the sphenoid, the cribriform plate and lateral masses of the ethmoid, the lacrymal, and the nasal processes of the superior maxillary bones.

Three-fourths of each parietal bone are represented by various forms of Wormian bones, varying in diameter from 3 mm. to 3 cm., while the remaining fourth consists of a single quadrilateral segment measuring 4 cm. by 8 cm., occupying the anterior superior angle. Bordering the coronal suture on either side below the larger segments are three or four of smaller size, ranging from 2 cm. to 3 cm. in diameter. The temporal ridges are indistinct or absent. On the inner surface the grooves for the meningeal arteries are well marked. The average thickness is 3 mm. to 4 mm.

The squamous portions of the temporals, together with the lower borders of the parietals, from which they are indistinguishable, present the most delicate tracing, in many bones the long interlacing processes being limited entirely to the outer layer.

The upper part of the squamo-occipitalis is formed entirely of Wormian bones.

The distribution by numbers in the different regions may approximately be given as follows: frontal bone, 12; parietals, each 40; temporals, each 25; occipital, 30.

Although so much of the cranium is composed of Wormian bones, yet the cranial anlage are well preserved, the principal sutures and bony areas being present and in their proper relations, showing that whatever general influences affected the skeleton, they were, in the skull at any rate, limited to osteogenesis and not of earlier origin or farther reaching in their effects disturbing the fundamental elements and interfering with the type of development as is observed in the perverted chondrogenesis of chondrodystrophia fœtalis and frequently seen in monsters.

The same may be said of the rest of the skull; all the bones are present with their usual relations, though the imperfect development of some produces considerable deformity, most marked in the recession of the face.

Recession of the Face. When considered with the fact that the second and third molars, and the left lateral incisors in the upper jaw, and the left third molar and lateral incisor in the lower jaw have never erupted, it is evident that the marked recession of the face, reaching its maximum at the teeth, is due to perversions in the evolution of the latter, with consequent pernicious effects on the development of the jaws, which, together with the bones resting upon them, give the face its outlines.

The great disproportion between the height and width of the posterior nares, the latter exceeding the former by fully 1 cm., gives a broadening effect which, with the incomplete dentition already noticed, stamps the face anatomically of the infantile type, the general deformity being particularly conspicuous because of the adult cranium.

In discussing the nature of the fundamental process which led to the remarkable hypoplasia and deformity of this skeleton, at least four distinct conditions must be considered, namely, rickets, cretinism, chondrodystrophia fœtalis, and osteogenesis imperfecta.

The studies of Stilling,[1] Hildebrandt,[2] and Harbitz[3] show very clearly that the disease called by Vrolik and by Stilling osteogenesis imperfecta, which previously in all probability was classed under fœtal rickets, is a definite, intrauterine process, the chief characteristics of which are great brittleness and softness of the bones, numerous fractures, and resulting deformities, due to as yet obscure disturbances of myelogenic and periosteal bone formation. The histological studies show that typical lamellar bone tissue and large trabeculæ are not formed.

"The trabeculæ are small, few in number, far removed from one another, and more or less irregularly arranged; in part they are without mutual connection. A continuous system of trabeculæ with lamellar arrangement, Haversian canals, etc., is absent." (Harbitz.) The number of cases is as yet small, and the observations seem to be limited entirely to the bodies of newly-born and very young children. The possibility of recovery from the disease has not been discussed to any extent, and the condition of the skeleton in the event of recovery and continued life cannot be determined from the facts at hand. It is noteworthy, however, that the disease is not necessarily fatal, because Hecker,[4] Bury,[5] Klem,[6] and Railton[7] have described cases two years, eight months, and one year old, respectively; and Harbitz is inclined to the belief that some of the instances of dwarfism previously referred to fœtal rickets, and now regarded as examples of chondrodystrophy, may have been cases of osteogenesis imperfecta. Gurlt[8] has noted that osteopsathyrosis (fragilitas ossium) occasionally seems to depend upon hereditary conditions, but its possible relation to osteogenesis imperfecta awaits future study.

The condition of the cranium in osteogenesis imperfecta is an interesting one. Vrolik,[9] J. Schmidt,[10] and Harbitz found that in their cases the calvaria consisted not of continuous bone, but of a mosaic of larger and smaller bone plates, which sometimes touched one another, at other times were united by bridges of periosteum and dura. In Stilling's case the cranium consisted of a membranous sac, with occasional bone spicules here and there. The great number of Wormian bones in the skull of the skeleton now described might well be attributed to such disturbances of cranial ossification. So far as the observations go there seems to be no disturbance at the basal synchondroses in osteogenesis imperfecta.

In the present case the condition of the cranium, the fractures (ribs, humerus), and the evident deficiency of periosteal and myelogenic

[1] Virchow's Archiv, 1899, cxv. pp. 357–370.
[2] Ibid., 1899, clviii. 426–444.
[3] Zeigler's Beiträge, 1901, xxx. pp. 605–628.
[4] Case abstracted by Harbitz, loc. cit., p. 611.
[5] Ibid.
[6] Ibid.
[7] Ibid.
[8] Handbuch der Lehre von den Knochenbruchen, 1862, I. Theil, p. 147.
[9] Cited by Stilling.
[10] Cited by Harbitz.

ossification in general, favor the notion that it concerns an instance of osteogenesis imperfecta surviving far into adult life. There is, however, relatively only little evidence of previous fractures in the bones of the skeleton. The old fractures in some of the ribs may have been the result of ordinary traumatisms. The number of fractures generally present in the cases described in the literature is usually so large that definite traces would be expected to persist should the patient survive. Virtually all cases of osteogenesis imperfecta so far described have died under one year of age, and it is not impossible that in survivors the traces of healed fractures and infractions eventually may be obliterated or represented by various thickenings.

Harbitz[1] mentions a dissertation by Ekman[2] that contains a detailed description of a family characterized by the occurrence of dwarfism and osseous fragility through three generations. The ancestor could not walk because of deformity; of his four children, one daughter was small and deformed, with curved arms and legs, and one son was a dwarf. This son had, with a healthy wife, a son that from earliest childhood was liable to fractures on the slightest provocation. He also had curved extremities. This man married a healthy wife and had two children, first a son, who had so many fractures during his youth that when full grown he could not move, and second a daughter, who likewise suffered multiple fractures from early childhood and always remained dwarfed.

While the general appearances of the body in this case may remind one at first glance of a cretin, especially because of the general dwarfing, there is absent the facial expression, the depressed nose, and the thick lips of cretinism, which probably may be ruled out because of the fair degree of intelligence apparently possessed by the individual during life. There is no myxœdema, and the dwarfing is not wholly symmetrical. The total or almost total absence of thyroidin would favor cretinism, of course, as does the practically complete obliteration of the normal structure of the thyroid.

It is difficult, perhaps wholly impossible, to determine the exact influence which the abnormal state of the thyroid may have exercised upon the man's general health and upon the process of osteogenesis, because of the lack of definite knowledge in regard to his past history and the absence of the evidence that might have resulted from the use of thyroiodin early in life. Perhaps the evil effects of the fibroid transformation of the thyroid were wholly alleviated by compensatory activity on the part of the hypophysis, the weight of which is considerably above the normal average and the structure of which seems fairly normal. The apparently intimate relations between growth of the

[1] Loc. cit.

[2] Dissertatio medica descriptionem et casus aliquot osteomalaciæ sistens. Upsaliæ, 1788.

skeleton and the physiological functions of the thyroid should stimulate to careful chemical and histological study of the thyroid in all instances of general disturbances of skeletal development. In chondrodystrophia fœtalis we lack information as to the chemistry of the thyroid, which often has been found abnormal in its appearances. In Harbitz's case of osteogenesis imperfecta (fœtus within four to five weeks of full term) the thyroid and thymus did not contain any iodine, but stress cannot be laid on that fact because iodine may be absent normally in the newborn.

The skeleton shows some features that might be explainable on the basis of a healed, severe rickets, such as the beaded ribs, the curvatures, and the flattening of the long bones, the spinal and pelvic deformities. The unusually large number of Wormian bones point to intrauterine disturbances of ossification in the cranial vault. In this case an attempt to trace the condition of the skull to rickets would place the disease at a very early period of intrauterine development, namely, at the sixth to the eighth week, and there seems to be little to warrant such an assumption. The occurrence of congenital rickets, meaning by that rickets which has run its full course before birth, is denied by most observers. As rickets heals the bones become abnormally dense and plump—exactly the reverse of the condition of this skeleton, in which there is also marked enlargements of the articular ends of the long bones. There is absence also of the peculiar deformities (pectus carinatum, funnel-shaped breast) of the thoracic cage, an absence the more significant in view of the profound changes in other parts of the skeleton. True rickety dwarfs usually present long arms, femoral and tibial curvatures. In this case the micromelia is rhizomelic. For these reasons I am inclined to believe that rickets in the ordinary sense cannot explain the case.

Osteomalacia hardly needs to be discussed extensively. As this disease subsides the affected parts may become more or less sclerotic. The shortness of the long bones and the condition of the skull are not explainable on the score of osteomalacia as generally understood.

A glance at the photographs shows that the man was not a true dwarf (microsomia), but a short-limbed or micromelic dwarf. The first general impression probably would be that it concerns an instance of chondrodystrophia fœtalis of Kaufmann or achondroplasia (Parrot). This disease, concerning which much has been written of late,[1] was formerly classed as fœtal rickets, which term even now is sometimes used expressing the same thing as chondrodystrophia. It is thought to have existed in ancient times, because the statues of the Egyptian god

[1] A fairly good review of the literature is given by Klein in Centralbl. f. allg. Path. u. Path. Anat., 1901, xii. 838–849.

Phtah and other deities are good representations of the external appearances produced by this disease.[1] Chondrodystrophia fœtalis affects especially the bones which arise in the cartilage in early fœtal life. Indeed, it is said to run its course between the third and sixth weeks, so that it would be stationary or cured when the child is born, while its effect upon the skeleton would remain permanent. The bones especially affected would be, then, those at the base of the skull, the ribs, the pelvis, and the long bones of the extremities. The bones formed entirely in the membrane, and those which, though formed in the cartilage, remain altogether or mainly cartilaginous until a late period of intrauterine life, are usually quite normal in size. Certain changes in the bones of the hands, especially the fingers, described by John Thomson,[2] William Turner,[3] and others, would seem to indicate that the disturbances of ossification may go on at a little later period. The lesions are usually symmetric, the micromelia is rhizomelic; there is some macrocephaly, "trident hands," and normal thorax.

The cause of the disease is wholly unknown. Perhaps B. Morpurgo's[4] observations on malacic and rickety changes in the skeletons of young white rats, produced by the injection of the cultures of a diplococcus, may prove of value in seeking for explanations of the osseous lesions in rickets, chondrodystrophy, and other diseases. In Morpurgo's animals the lesions at the epiphyseal zones of ossification were similar to those seen in rickets. Regnault[5] claims that "chien basset" (basset hound) depends upon a disease that corresponds to chondrodystrophia or achondroplasia (Parrot), as the condition is termed in the French literature, in which it also seems to cover osteogenesis imperfecta of the Germans. The peculiar race of dogs referred to has resulted, he says, from the fixation by heredity of an anomaly by means of artificial selection. Leblanc[6] and Apert[7] also believe that achondroplasia occurs in animals. "Maitons aneons" (descendants of certain sheep in Massachusetts), "bœufs notos," "veaux-bouledogues," "veaux-tortues," and "chien basset" are the examples given. But in no case has this claim been substantiated by careful histological study. And Cestan points out that here it concerns veritable races capable of transmitting the peculiarities to descendants, whereas achondroplasia in man occurs usually in isolated cases, which rarely transmit the disease, the children, if any are born, being usually normal. History records that the efforts of

[1] Harbitz, loc. cit., note on page 637. Charcot and Richer: Des difformes et les malades dans l'ast, Paris, 1889, p. 12.

[2] Edinburgh Medical Journal, 1892-93, vol. xxxviii. pp. 1109-1113.

[3] Practitioner, 1899, vol. lxiii. pp. 263-277.

[4] Centralbl. f. Path., 1902, xiii. p. 113.

[5] Bull. et Mem. de Soc. anat. de Paris, 1901, lxxvi. pp. 386-389.

[6] Compt. rend. de Soc. de Biol., 1902, liv. 88, 89.

[7] Ibid., 127-129, and Nouvelle Iconographie de la Salpêtrière, 1901, xiv. 290-298.

Catherine de Medici and others to breed dwarfs did not succeed. Pourak[1] and others, however, have described an instance of apparent transmission of achondroplasia from parent to offspring.

Leblanc[2] claims that chondrodystrophy often is associated with myxœdema, and that the thyroid probably is the seat of primary disturbance. Nasan[3] also ascribes achondroplasia to thyroid dystrophy. This claim is not borne out by the observations of Cestan,[4] who, in a richly illustrated article, describes a case of chondrodystrophy in a girl, aged nine and one-half years, in which thyroid treatment was given a thorough trial for nine months but without effect, and Marie,[5] who, in two instances, failed to obtain any benefit from thyroid extract. Christopher[6] also failed to secure any effect with thyroiodin in one case, and Legny and Regnault[7] found the thyroid normal in three chondrodystrophic fœtuses. And then there is the fact that the lesions of chondrodystrophy develop in the earliest months of fœtal life before the thyroid is fully developed.

The histological changes which have been studied thoroughly by Kaufmann[8] and others vary more or less according to the form or variety present, of which Kaufmann recognizes three, namely, the malacic, the hypoplastic, and the hyperplastic. Of the latter only three or four cases are described.[9] Whether chondrodystrophia malacica, hypoplastic, and hyperplastic are all expressions of the same fundamental disturbance or process may well be doubted. As indicated by the terms used the epiphyseal and other cartilages may be the seat of defective development, of softening, or of overgrowth, the latter being irregular; in all cases normal ossification and growth in length fail to take place, as no columns of cells are formed as normally. Ingrowth of the periosteum at the lines of ossification may occur, and this may also prevent growth in length.[10] The shafts of the long bones increase in growth from periosteal ossification, which goes on normally in this disease, and the bones become more or less irregular, and, as a rule, thick and plump, hard and sclerotic, as well shown in radiographs, the internal architecture being abnormal. Deformities may arise. Premature synostosis at the base of the skull, and a more or less depressed insertion of the nose, may result.

Two types of physiognomy are spoken of, the cretinoid (premature

[1] Cited from Nouv. Arch. d'Obst. et de Gyn., 1889–90, by Thomson, loc. cit.
[2] Loc. cit. [3] Rev. de Neurologie, 1901, p. 549.
[4] Nouvelle Iconographie de la Salpêtrière, 1901, xiv. 277–289.
[5] Presse Medical, July, 1900, vol. iv. [6] American Medicine, June 7, 1902.
[7] Compt. rend. de Soc. de Biol., 1902, liv. 567–568.
[8] Sogenannte Fœtale Rickets (Chondrodystrophia Fœtalis), Berlin, 1892; Zeigler's Beiträge, 1893, xiii. 32–64.
[9] Kaufmann, Johannesen, Klinger, Joachimsthal.
[10] Collmann. Virchow's Archiv, 1901, clxvii. pp. 1–13.

synostosis of the "os tribasilare"), and one marked by flattening of the whole nose rather than retraction of the root of the nose. In Johannesen's case there was no premature basal synostosis.[1] And Regnault also found the cranium normal.[2] The bones of the calvaria have been found generally normal (Harbitz), or there has been present an exquisite craniotabes (Klein). There may be more or less beading at the costo-chondral junctions. While the trunk is more nearly of the normal length, the extremities are too short, and the skin and soft parts here seem too large. In the hyperplastic form the epiphyseal ends are irregularly swollen. The pelvis is small and deformed, the cotyloid and glenoid cavities may be aplastic, and lordosis seems to be marked; it is explained as due to statical reasons, the weakness of the femurs throwing the weight of the body in front of the normal line. Regnault,[3] in a chondrodystrophic fœtus, found the vertebræ involved. Because the infants affected with this strange disease usually die before or shortly after birth (of Kaufmann's thirteen cases only three were born alive), not so very much has been learned as yet concerning the condition of the bones in those that survive. John Thomson[4] has described two living cases, aged thirty-nine and thirty-six years, the photographs of which in their general features are not unlike the appearances in this case, the noses, however, being much more depressed. The palates were high and arched. There were kyphosis and lumbo-sacral lordosis, and the limbs were half as long as they should be. The hands had a characteristic spade-like form, being broad and short, the fingers far apart, fusiform and thick, the index and middle fingers turning toward the radial side, the ring and little fingers to the ulnar ("main en trident"). This condition of the hands was absent in this case. Parrot[5] reports a girl, aged seven and one-half years; William Turner one aged ten years; Boeckh mentions a chondrodystrophic woman whose father and several relatives were similarly affected, and Pourak describes a micromelic female dwarf who became pregnant twice, one of the children showing the same condition as the mother. The disease is probably more frequent than the scanty reports in the literature may be regarded as indicating. The number of cases described has multiplied rapidly of late, especially in French and also in American literature. There is Baldwin's case, to which reference will be made shortly. Osler[6] describes two cases in brother, aged eleven and a half years, and sister, aged sixteen years. John Lovett Morse reported to the American Pediatric Society at its last meeting (1902)[7] an in-

[1] Reference cited by Klein, loc. cit.
[2] Bull et Mem. de Soc. Anat. de Paris, 1901, lxxvi. pp. 419–421, 424–426, and 597–599.
[3] Bull et Mem. de la Soc. d'Anat., 1901, lxxvi. pp. 559–560.
[4] Loc. cit.
[5] Loc. cit.
[6] Trans. Congr. Am. Phys. and Surg., 1897, vol. iv. pp. 190–192.
[7] American Medicine, June 7, 1902.

stance in a child that died at four months. In the discussion Griffith mentioned two cases, Holt one case, and Christopher one case. Abt[1] has described a typical instance in a boy of twelve years, under the title of "Ricketts." This case is interesting, also, because the coccyx was directed forward so as to cause pain on sitting. Cestan,[2] Apert,[3] and others also describe and illustrate living cases. In Cestan's case the micromelia was rhizomelic, the humerus and femurs being most affected. Apert notes that one not seldom sees cases in the streets. Undoubtedly many follow circuses and theatrical troupes. I have seen three apparently typical cases—two men and one woman—on the streets in Chicago, but I was unable to obtain any facts in regard to their history and exact condition. I also know a farmer in Wisconsin who is a micromelic dwarf, four feet and eleven inches in height, and 145 pounds in weight. The fingers of the left hand show the characteristic trident deformity, the fingers on both hands being more nearly the same length than normally and broad. The relative shortness of the limbs is especially marked in the lower extremities. He wears a No. 7½ hat, and the head appears large, the nose being well developed. He is a good worker and presents an athletic appearance, and is a man of intelligence. He was born of healthy parents of usual size; there is no other dwarf in the family. The appearance of chondrodystrophic adolescents and adults are so characteristic that, as Marie[4] says, if one does not recognize achondroplasia it is because he does not know the disease.

J. P. Baldwin,[5] in 1890, reported a successful Porro-Cæsarean operation upon a typically rachitic dwarf, weighing 100 pounds, and 47½ inches tall. The illustration accompanying the report shows well the characteristics of chondrodystrophy. The child is stated to have inherited the peculiar deformity of the mother, but no details are given.

Joachimsthal[6] used the X-ray in the study of dwarfism and allied conditions. In an instance of hyperplastic chondrodystrophy in a girl, aged twelve years, the epiphyses were cartilaginous and swollen, and there were certain peculiar appearances at the ends of the shafts due to the ingrowth of the periosteum, he thought. There was in Joachimsthal's case no growth in length in fifteen months. It is noteworthy that almost without exception those who survived beyond infancy are said to have been of average or more than average intelligence. Many are vigorous physically.

Virchow[7] has touched upon the conditions here discussed at various

[1] Archives of Pediatrics (reprint). [2] Loc. cit. [3] Loc. cit.

[4] Presse Medicale, July 14, 1900, where he gives an excellent description of chondrodystrophy in adults.

[5] Medical News, 1890, vol. lvii. pp. 138–141.

[6] Deut. med. Wochenschr., 1899, xxv. pp. 269–271 and 288–290.

[7] Virchow's Archiv, 1901, clvi. pp. 192–193; Ibid., 1883, xciv. p. 183.

times. He objects[1] to the term dystrophia, introduced by Kaufmann, because the condition imperceptibly shades into a pronounced developmental anomaly (missbildung), which, in its most characteristic form, is represented by phokomelia (Saint Hilaire, 1836). It concerns rather a profound disturbance in the formation of parts affecting not only cartilage, but also soft parts and bone. (Whether the smallness of the internal organs in cases like the one now reported is due to fundamental genetic disturbances or is secondary to skeletal hypoplasia cannot be determined off hand, and the question merits study.) Congenital rickets leads step by step to phokomelia. The name suggested by Kaufmann, and so generally adopted by others, puts into the foreground a single local disease which in turn is referred to a nutritive disorder. He is inclined to think that the name "fœtal rickets" may yet survive chondrodystrophy. As long ago as 1853 Virchow discussed the question of fœtal rickets upon the basis of a specimen in the museum at Wurzburg.[2]

Summary. In the foregoing is described a fairly symmetric micromelic dwarf, aged forty-five years, presumably of fair intelligence; with a fibroid thyroid without any demonstrable thyroiodin; with a relatively large cranial vault made up of 172 Wormian bones, but without any evidence of premature ossification of the synchondroses at the base of the skull; with marked curvatures of the spinal column; with old fractures of many of the ribs and of the left humerus; with great deformity of the pelvis; with curvatures of most of the long bones, which are relatively short, the articular ends being swollen into irregular globular masses; with a general and pronounced osteoporosis; and with absence of trident fingers.

Cretinism or rickets or osteomalacia in all probability is not wholly responsible for the changes present in the skeleton. Taking all the facts and conditions into consideration, it must be acknowledged that the case presents some features best explainable on the score of osteogenesis imperfecta, others best explainable on the score of chondrodystrophia fœtalis, but as for reaching definite conclusion, it is unfortunate that the picture of either of these two diseases, as now understood, is incomplete in some essential particular; and, furthermore, that nothing is known of the man's earlier history. There is absent the premature synostosis of the cranial base of chondrodystrophia, and the bones of the extremities are not as plump and hard as would be expected in this disease. While many of the peculiar features correspond well with one's conception of a healed or arrested osteogenesis imperfecta, yet there are no observations on record of the bones in survivors from this disease, and there is relatively but little evidence in this case of its

[1] Zeitschr. f. Ethnologie, 1898, xxx. p. 55.

[2] Virchow's Archiv, 1853, v. 409–508.

most striking characteristic, namely, extensive multiple fractures. Were a history obtainable of great brittleness and softness of the bones at birth and for some time afterward, the evidence in favor of osteogenesis imperfecta would be materially strengthened. Undoubtedly the porosis of many of the bones in the skeleton may be ascribed to the disuse incident to the deformities, whatever the real nature of the fundamental cause. In this way a more or less atypical chondrodystrophia hyperplastica might have been succeeded by osteoporosis rather than osteosclerosis, as seems to be the rule, but the porosis is so marked and so general as to suggest general genetic disturbances. A combination of osteogenesis imperfecta with chondrodystrophia, complicated later in life by genuine rickets, might also be suggested. As the matter now stands, final conclusion seems unattainable, and it must suffice to place the case upon record as one example of the grave changes that may be produced in the skeleton by obscure and interesting processes, the real cause and nature of which we do not understand.

A NEW METHOD OF CORRECTING FLEXION DEFORMITY AT THE KNEE-JOINT.[1]

By Royal Whitman, M.D.,
of new york.

No deformity is more difficult to correct satisfactorily than fixed flexion at the knee-joint in the class of cases in which one aims to straighten the limb by movement within the joint and to preserve or to increase its range of motion.

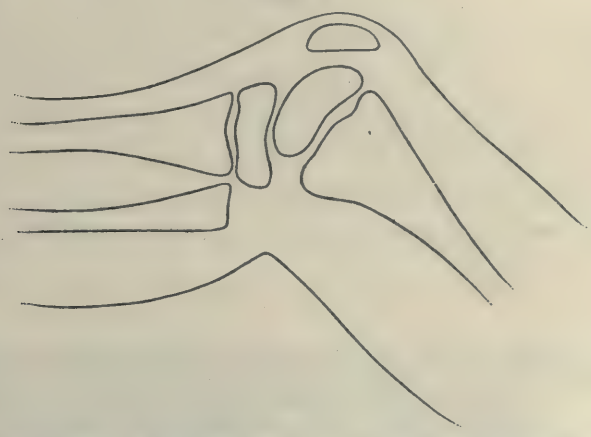
In the attitude of flexion the relaxation of the ligaments permits a considerable degree of mobility, a mobility that is increased if the capsule is distended with fluid or if the ligamentous support is weakened or destroyed. Thus flexion deformity is often complicated by backward displacement and outward rotation of the tibia upon the femur. (Fig. 1.)

In the movement from extension to flexion at the knee the articulating surface of the tibia glides backward from the inferior to the posterior portion of the condyles of the femur. If flexion persists, as it practically always does in joint disease, there is subsequent contraction and shortening of the flexor muscles and of the fibrous structures on the posterior aspect of the joint. In many instances there is also an actual enlargement of the lower extremity of the femur, particularly of the inner condyle, and there are other secondary changes

[1] Read at the meeting of the Harvard Medical Society, December 27, 1902.

within and without the joint that tend to fix the deformity. When, therefore, the attempt is made to straighten the flexed leg the tibia is prevented from gliding forward, and, unless the obstacles to this movement are overcome, the extension is effected with the anterior part of the tibia in the line of the centre of the femur (operative sub-

FIG. 1.

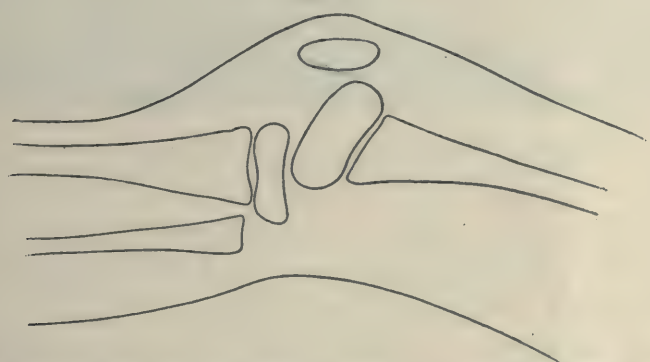


Flexion deformity at the knee-joint, with slight subluxation of the tibia.

luxation). This subluxation is often induced by the attempt to correct deformity, and it is almost inevitably increased if it be present already. (Fig. 2.)

Posterior displacement is an unsightly deformity, and it limits still more, whatever capacity for motion may have escaped the disease. It is also a direct source of weakness and discomfort.

FIG. 2.

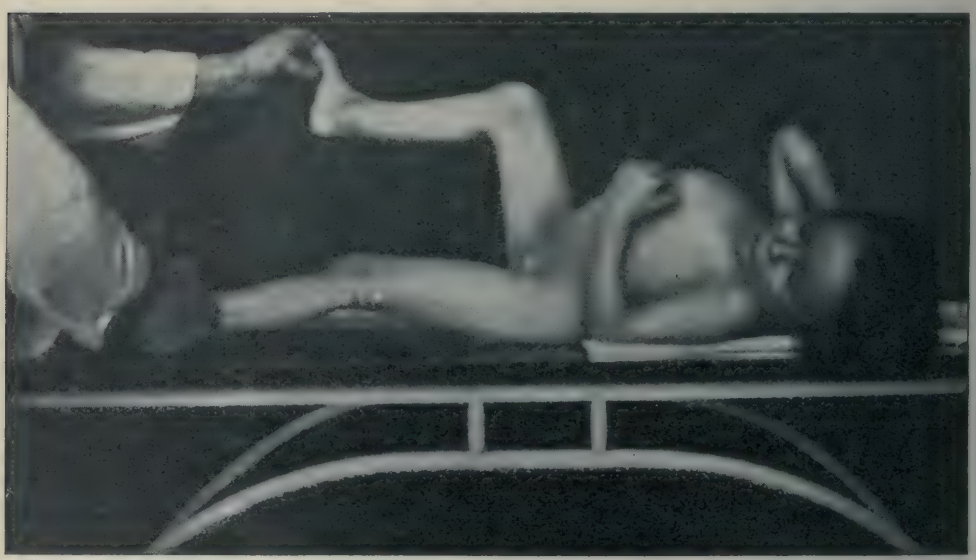


After forcible correction, showing the increase of the posterior displacement. Drawings from the X-ray photographs of an actual case.

Operative subluxation is most often induced or increased by direct forcible straightening of the limb. This is the means usually employed to correct the deformity, because other methods are so unsatisfactory. For example : traction, so effective when flexion is due simply to muscular spasm, is quite inadequate for the treatment of resistant cases. The Bradford-Goldthwait genuclast, a useful appliance for cor-

recting this distortion in older subjects, is not at all suitable for the treatment of children, the class in which it is most common. In fact, osteoclasts of any form should not be employed, because they are more likely to cause fracture or epiphyseal separation than to overcome the resistance of the tissues. The modified Billroth plaster splint, in which the centre of motion is placed, by means of the appliance of Stillman or Bratz, above and in front of the joint, and in which the limb is straightened gradually by wedging the two halves of the plaster apart, is, perhaps, the most satisfactory treatment; but if subluxation is not increased it is certainly not reduced as the limb is straightened. Special machines of complicated design have been devised, but these are excluded from consideration by their costliness, and I know of none that offers any particular advantage over the Billroth appliance, even if it were at hand.

FIG. 3.



Right angular flexion, with subluxation, the result of tuberculous disease. The patient has Pott's disease and marked deformity of the spine as well.

However the means employed to overcome deformity differ, they are alike in this, that the tibia is used as the lever, while the femur is a fixed point.

During my last term of service at the Hospital for Ruptured and Crippled, confronted by a number of difficult cases of this class, it happily occurred to me that if the ordinary process of correction were reversed, that is, if the femur were made the lever and the tibia were fixed, the danger of subluxation might be avoided; for, as is evident, if a part be fixed it cannot be displaced. On the other hand, extension of the femur on the fixed tibia would tend to force its lower extremity backward, and thus to lessen the degree of subluxation if it were present.

In order to straighten a contracted knee by this method the patient, thoroughly anæsthetized, is turned face downward upon the table. Pillows are then placed beneath the abdomen to accommodate the deformity; that is, the trunk must be elevated sufficiently to permit the anterior surface of the tibia to rest evenly upon the table. (Fig. 3.) This attitude offers no particular difficulty in young subjects, and it has the great additional advantage that the contracted part is uppermost and directly under observation. The operator then holds with one hand the head of the tibia firmly against the table, and with the ulnar border of the other begins forcible massage upon the contracted hamstrings, after the method employed in overcoming the resistance of the adductors in the operation of reduction of congenital dislocation of the hip. (Fig. 4.) In this forcible massage pressure is begun half-way up the thigh, thus exerting a certain extending force. As the resistance lessens the trunk is lowered and the assistant begins to press the thigh

FIG. 4.



Illustrating the method of supporting the body and fixing the tibia before straightening the limb. The folded sheet indicates the degree of subluxation present.

gently downward toward the table, rhythmically stretching and relaxing the resistant tissues, but never with sufficient force to lift the head of the tibia, which is firmly fixed to the table by the operator, reinforced, if necessary, by the hand of an assistant.

If the contraction is of long standing, and especially if subluxation is present, one should not attempt to complete the correction at the first operation, and in certain instances preliminary division of the shortened flexor tendons may be required. When the deformity is corrected or when it is considered advisable to discontinue the operation, a plaster bandage is applied, or, if it is thought desirable, adhesive plasters may be attached to the limb, and strong traction by weight and pulley may be employed. When the flexion has been overcome, the knock-knee, which is usually present, can be easily corrected by gentle force. As the disease, in the majority of cases in which this method is employed, is of a chronic or a quiescent character, a Thomas

knee-brace, provided with traction straps, is finally adjusted, and the after-treatment is conducted in the usual manner.

The principles of this method might be carried out by mechanical devices, but I prefer manual force whenever possible, as it is much less likely to be abused, and, as has been stated, the alternate tension and

FIG. 5.



After forcible correction by the method described. Compare with Fig. 3.

relaxation combined with forcible massage is not only far safer, but it is far more effective than a continuous force of greater intensity.

It is of interest to note that pain following the operation, provided the limb is fixed in a plaster bandage, is slight or absent, nor is there that degree of local reaction that is often observed when gradual reduction is attempted by means of braces and bandages, the so-called

gentle method. This indicates that it is persistent tension on contracted parts rather than the correction of deformity that excites the reaction.

The treatment here recommended is, of course, hardly necessary when the flexion is due to simple muscular spasm; on the other hand, it may be applied to resistant deformity from causes other than tuberculous disease with equal advantage, for example, after gonorrhœal, typhoidal, or other forms of infectious arthritis.

There are cases in which the changes within the joint make it impossible or inadvisable to straighten the limb completely by this or other means. In such cases it is advisable to perform an osteotomy just above the joint; the limb is then straightened and whatever motion is present is thus transferred to a point at which it will be of greatest use.

PRONATION OF THE FOOT.*

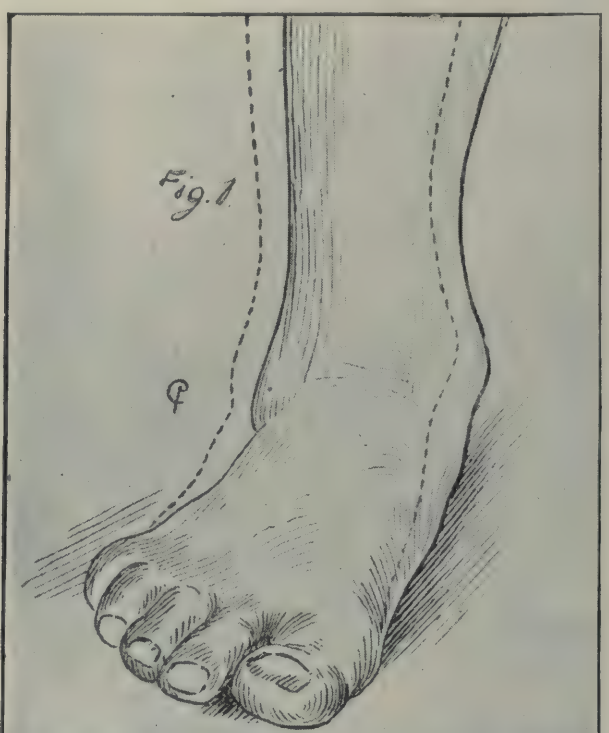
By E. J. Huhner, M.D.,
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This paper will deal entirely with a pathological condition and not with a physiological function. Pronation is not to be confounded with flat-foot, from which it is distinct. Lovett and Cotton[1] define pronation as "that vicious attitude of the foot in which in habitual standing position it rolls over inward, the inner malleolus projects, and abduction of the front part of the foot occurs."

It is also known as weak foot and weak ankles, and is often an exaggerated or faulty use of a normal position. The cause of pronation is the pressure of the body-weight upon the foot, lifting and carrying heavy burdens. Rheumatism, gout, and rachitis are predisposing causes. Stiff-ankle shoes, by producing weakness of the parts, according to Taylor,[2] cause pronation. Wilson[3] claims comparative freedom from this malformation is noticeable in those who wear sandals or go barefoot. Lovett and Dane[4] are inclined to the belief that modern footwear deprives the foot of a support and the tendency to pronation is favored. The voluntary adduction of the normal foot (Whitman[5]) is about 30°; abduction is somewhat less. The angle of inclination of that part of the foot anterior to the mediotarsal joint was found by Roberts[6] to average in males 34.8°, and in females 31.5°. Abduction, with some pronation, is the normal position when the body-weight is sustained without muscular exertion. This, according to Sampson,[7]

*Read before the Orleans Parish Medical Society, November 22, 1902.

" becomes pathological when excessive or used in other or all attitudes." Abduction is the position of weakness and rest; adduction, that of strength and activity. As to the diagnosis of pronation, the old method of taking imprints on smoked paper, etc., is almost universally condemned as being worthless, except in advanced cases or for verification of other diagnostic measures. The method of Lovett and Cotton[1] to determine the amount of rotation of the astragalus is excellent. The horizontal rotation of the malleoli is determined and used as an index. These measurements, as the originators state, are fairly accurate, though not mathematically so, " as no measure of pronation can be." The amount of deformity may be determined by the plan



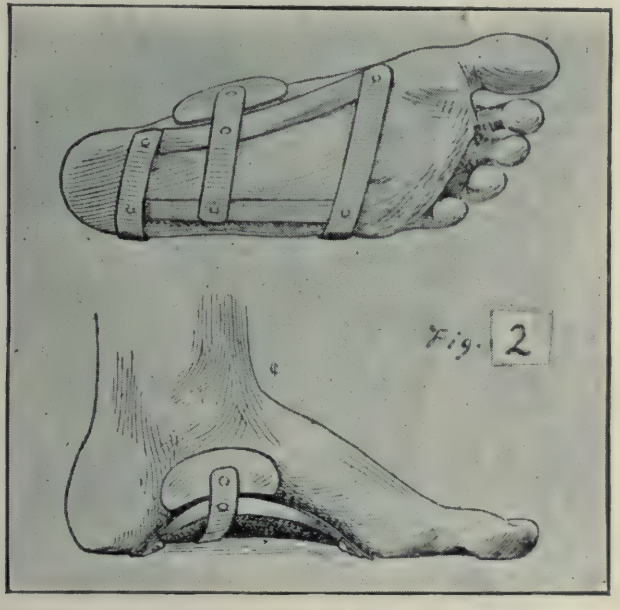
Pronation (from photograph). Position of correction shown in broken line

suggested by Young[8] of taking several photographs upon the same plate with the weight off and on the foot. Briefly stated, the mechanism by which weak foot is produced is as follows:

The head of the astragalus rotates inward and backward, its body forward and outward. This rotation causes the internal malleolus to move backward and the external forward; the front part of the foot is abducted as a whole, and the calcaneum rotates toward a valgus position. In the treatment of pronation strict attention must be given to the footwear. The inner edge of the shoes should be straight; sufficient space is necessary to permit spreading of the toes. Increase adduction: For this purpose Sampson[7] employs a toe-post, fitted in the shoe, between

the great and second toes. Raise the inner side of the shoe. According to Whitman,[9] this frequently is all that is necessary. Tip-toe exercises are given to strengthen the adductors and external rotators of the foot. Often mechanical support is necessary. The ordinary metal plates are objectionable, because they are injurious, interfering as they do with muscular action and inducing atrophy of the muscles of the sole, and, more, they do not directly correct the pronation. Ankle supporters inhibit motion and induce atrophy. Lovett and Cotton[1] have devised an apparatus which reduces these objectionable features to a minimum.

It is light, allows free muscle action, and corrects the distortion. Its most important action is derived from the plate, below the tuberosity of the scaphoid, which exerts elastic pressure outward.



In an examination of the feet of 132 white persons, recently made by me, the result demonstrated the frequency of pronation. The ages of these subjects ranged from eight to seventy-two years; 82 were females and 50 males. Of the 50 males, 9 exhibited pronation in the right foot, 16 in the left foot, and 7 in both feet; in other words, 32 (64 per cent.) were so afflicted. Of the 82 females, 14 presented pronation in the right foot, 18 in the left foot, and 33 in both feet—a total of 65 (about 79.2 per cent.). Of 69 male and female negroes examined, the feet were pronated in about 85 per cent. The excessive occurrence of this deformity in negroes is explained by their occupations, which entail, in the majority of them, almost constant standing and the carrying of heavy burdens. In the cases in the white subjects, abduction determined by Roberts' method varies from 6° to 20°. In three cases the amount of rotation of the astragalus was

found to be 58°, 63°, and 68°, respectively. Pain was very severe in 8 cases. According to my observations, pronation of the feet is more frequent in females than in males. The explanation of this is to be found in the feminine footwear—that is, shoes with high heels, narrow toes, and curved so as constantly to abduct the foot.

In conclusion, I desire to thank Mr. George Augustin for his valued assistance in my search for references, and Dr. John Ridlon, who so kindly gave me permission to use the illustrations in the *Transactions of the American Orthopedic Association.*

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A CASE OF ANEURISM OF THE TRANSVERSE PORTION OF THE AORTIC ARCH IN A GIRL OF NINE YEARS, WITH TABLE OF REPORTED CASES UNDER TWENTY YEARS OF AGE.

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THE patient presented, who is the subject of this paper, was brought to St. Christopher's Dispensary on October 19, 1902, for treatment for pain in the left wrist, and a cough which she had had for some weeks.

Violet B., aged nine years.

Family History. Parents living and healthy; no history of rheumatism or specific infection. Two other children living and well. The oldest child died from pertussis shortly after the birth of the patient. At birth there were no signs of specific disease; there was no cyanosis directly after birth, and the labor was not remarkably severe.

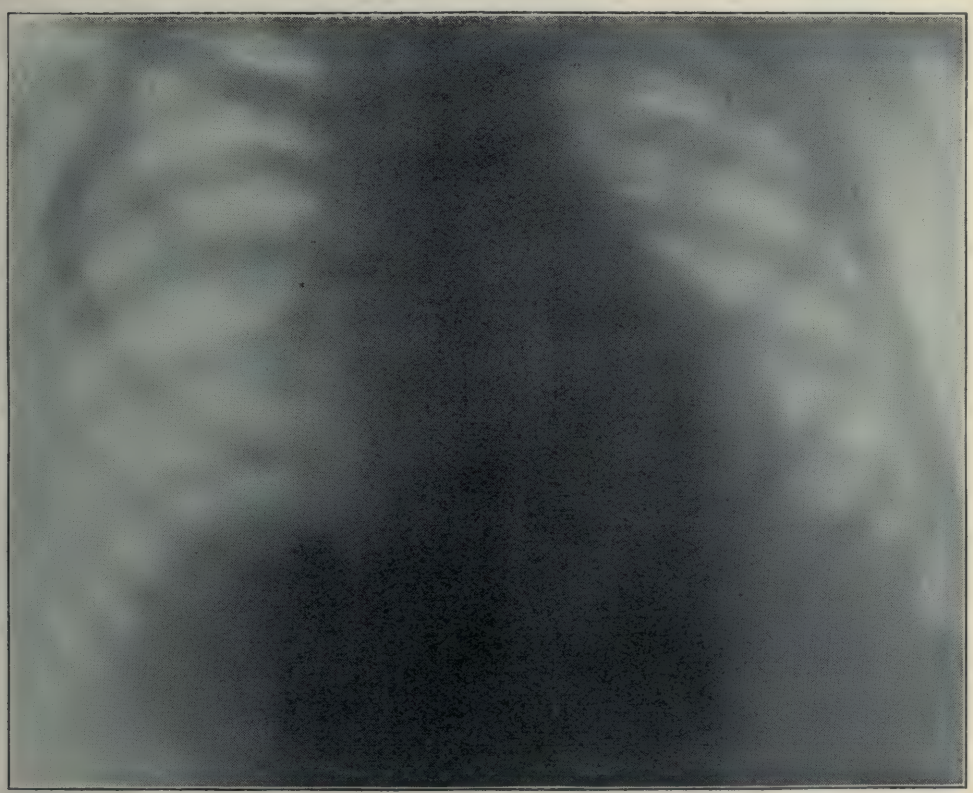
Previous History. When nine days old she had an attack of pertussis which lasted for seven weeks. Until three years of age she had no illness, but at that time had a second attack of pertussis which was very severe, and the cough is said to have lasted for six months. When four years old she is thought to have had rheumatism, as in the extremities there were vague joint pains, which have continued at intervals. Some heart trouble was diagnosed at this time. Typhoid fever at seven; and last July she had measles.

Present History. The cough is rather moist, with at times a clear, watery expectoration; occasionally it is hard and quite brassy in character. There is slight pain under the sternum if the cough is severe. The joint pain, which at present is confined to the left wrist, is sharp

in character, lasting only a short time. With previous attacks there has also been pain in the legs. Sweating is always bilateral; she flushes up on exertion, but equally. Her hands and feet are cold and rather clammy to the touch, becoming more so when frightened, when she trembles and becomes pale, but *never cyanosed.* The negative symptoms are rather instructive, as there has been no œdema, ascites, dyspnœa, palpitation of the heart, headache, or vertigo.

Physical Examination. The patient is tall, rather thin, dark rings about eyes; some protrusion of eyeballs; pupils equal, no contraction or dilatation; sclera, lips, and tongue pale. The superficial veins, especially those of the upper part of the chest, neck, face, and arms, are quite markedly engorged. There is no clubbing of the fingers. Visible

FIG. 1.



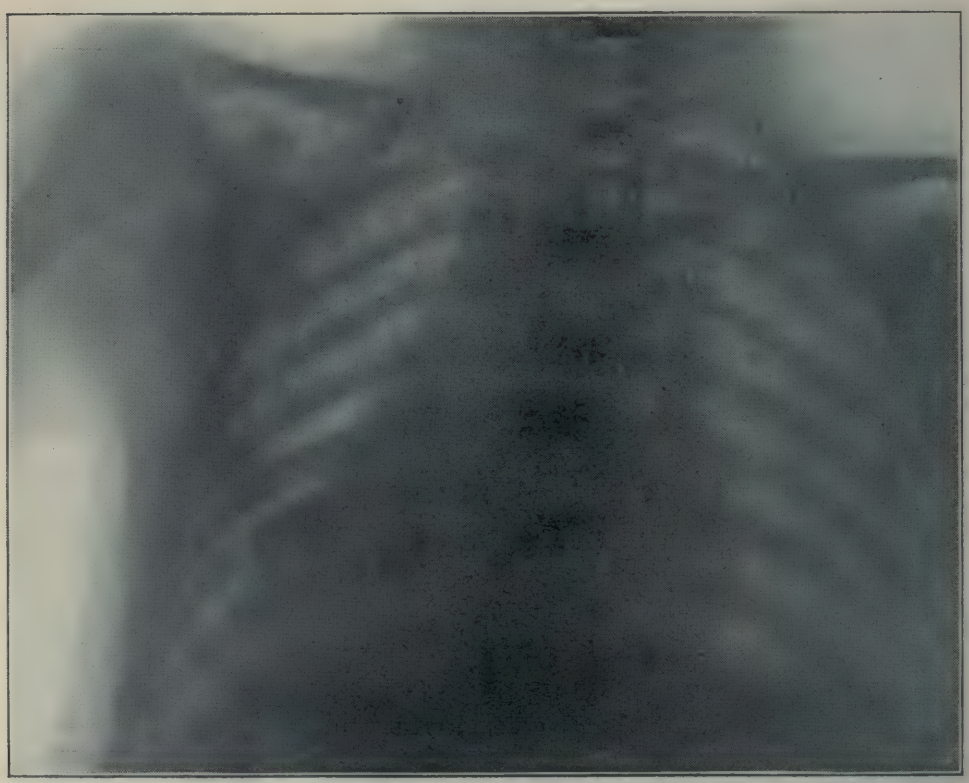
wavy pulsation from the second to the fourth intercostal space on the left side, with the maximum pulsation in the third interspace in the midclavicular line. Visible pulsation also in suprasternal notch and the vessels of the neck, slightly more marked on the right side.

Palpation. Thrill, systolic in time, with the maximum intensity in the first right intercostal space, one-half inch from sternal border, extending to the midclavicular line, downward to the third rib and upward into the vessels of the neck; well marked in suprasternal notch, where a pulsating mass can also be palpated. On the left side over the first and second intercostal spaces outward to the midclavicular line. At the apex there is also a slight systolic thrill, which does not seem to be connected with the above. The radial pulses are small, weak, and easily compressible, but regular, the left pulse being slightly slower and

weaker than the right; no capillary pulse. Tracheal tug fairly well marked. The pulsation of the abdominal aorta is not palpable. Dr. Osler[1] remarks that this is a physical sign of large thoracic aneurisms which he had not seen noted.

Percussion. A dull note is found extending from one-half inch on the inner end of the right clavicle to one-quarter inch on the left clavicle; downward to the second rib on the right side and blending with the cardiac dulness on the left. Cardiac dulness extends from the second interspace to the apex under the fourth rib, and one-quarter inch without the midclavicular line; the right border one-half inch to the right of sternum and the left border just without the midclavicular line.

FIG. 2.



Auscultation. There is heard a loud, harsh, rasping murmur, synchronous with and obliterating the first heart sound; loudest over the first right intercostal space close to sternum and in the suprasternal notch. Over the second rib and second right intercostal space the first sound is also obliterated, and the second heart sound markedly accentuated, the murmur ending just before the second sound. Over the first and second left intercostal spaces the first heart sound is not obliterated. The murmur is transmitted down the sternum almost to the xiphoid cartilage; to the right and left axillary region, over both sides of the chest, posteriorly to about two inches below the angles of the scapulæ; less distinctly over the body of the heart. Murmur heard loudly and almost reduplicated over the right carotid, less loudly and single over the left; well marked over entire supraclavicular regions, especially

[1] Practice of Medicine, second edition, p. 710.

on the right side; heard over the trachea. At the apex is heard a systolic murmur distinct from the above, being softer and more blowing, following the first sound, while there is also a very soft, blowing, presystolic murmur. The abdomen is flaccid; no tenderness on palpation. Not tympanitic. The spleen, liver, and kidneys are not palpable.

In this case the cause of the aneurism is a difficult one to determine. It may have been induced by an attack of pertussis shortly after birth, when by severe paroxysms of coughing the wall of the aorta may have been partially ruptured, or at least weakened, and in time the pressure of the blood current on this weakened or torn portion caused dilatation and aneurismal formation.

Again, atheromatous change may have resulted from the rheumatic attacks.

Table I.—Aneurisms in Early Life.

a. Thoracic Aorta.

Case 1. (R. T. Smith, Lancet, 1834, i., 626.) Ascending aorta. Male, aged sixteen years. Diseased aorta, thickened mitral valves. Thinning of walls of aorta, no morbid growth. Sudden onset, sharp, piercing pain in region of heart after having ascended a ladder, followed by insensibility, cyanosis, and death in a few hours. Aneurism, size of walnut, from ascending aorta ruptured into pericardium. Cause: Loss of elasticity in wall, dilatation, rupture on exertion.

Case 2. (Mr. Hutchinson, Transactions of the London Pathological Society, 1854, v., 104.) Aortic arch. Female, aged four years. Heart and vessels normal. No previous symptoms. Ill ten days with acute idiopathic pericarditis. Aneurism thought to have originated as an abscess and ulcerated into the aorta, the lining membrane of which was healthy to the edges of aneurismal sac. Size of two chestnuts side by side.

Case 3. (M. Roger, Bull. Soc. Méd. d'Hôp. de Paris, 1863, 499.) Aortic arch. Female, aged ten years; heart normal. No serious illness, rheumatism or scarlet fever. Dyspnœa on exertion for five years. First suffocative attack when eight years old; last one five weeks before examination, lasting all night, with extreme dyspnœa, hanging tongue, pallid face, and cyanosed lips. Dulness in first left intercostal space, size of a two-franc piece. No thrill or visible pulsation. Loud systolic murmur, not obliterating heart sounds. Patient passed from observation.

Case 4. (Moutard-Martin, Bull. de la Soc. Anat., 1875, 775.) Ascending aorta. Aged two years. Heart hypertrophied; some atheromatous patches in aorta. Family history negative. Dyspnœa for several months. Intense murmur with first sound at base of heart, heard also throughout thorax. Pulse large and compressible. Death due to hemorrhagic smallpox. Pericarditis present.

Case 5. (G. Thibierge, La France Médical, 1881, ii., 913.) Ascending aorta. Female, aged seventeen years. Aortic valves diseased. Aorta dilated and a few small, discrete fatty patches in wall. Family history negative. Four months before had fever, chills, palpitation of heart, emaciation, extreme grayish pallor, pain in chest, which continued. Visible carotid pulse. Systolic thrill at apex, in first right intercostal space, and in carotids. Corrigan pulse. Loud systolic murmur at base, transmitted throughout thorax. At apex a softer systolic murmur apparently independent of first. In right carotid a strong double systolic murmur, single on left side.

Case 6. (N. Moore, Transactions of the London Pathological Society, 1882, xxxiv., 71.) Ascending aorta. Female, aged five years. Vegetations on the tricuspid, aortic, and mitral valves. Arteries normal. Death due to tubercular meningitis. Aneurism from the posterior aortic wall; in it several small endarterial growths.

Case 7. (Sanné, Rev. Mens. de l'Enfance, 1887, 56.) Ascending aorta. Male, aged thirteen years. Heart hypertrophied, aortic valves diseased. Thinning of walls of aorta, with atheromatous patches. Ill for six months, apathetic, dyspnœa, pallid face, cyanosis, extremities cold and clammy. Pulse large but compressible. Thrill over the pericardial region up to right

clavicle. Loud systolic murmur at base, softer diastolic murmur. Death due to asphyxia. Aneurism the size of a small nut.

CASE 8. (Rie, Wiener medicinische Wochenschrift, 1889, xxxix., 556.) Ascending aorta. Female, aged five years. Heart normal. Of two years' duration; palpitation on exertion; pulsation in second and third right intercostal spaces, marked thrill and loud systolic murmur over the same area. Radial pulses small, easily compressible, equal and synchronous.

CASE 9. (A. Pendin, St. Petersburg med. Wochenschrift, 1890, vii., 195.) Ascending aorta. Female, aged twelve years. Heart normal. Fall when six years old, struck right side, causing pain, which continued. No dyspnœa, cough, or hemorrhage. Slight bulging of right chest between second and fifth ribs; dulness over same area with expansile pulsation. No murmurs, but two clear sounds, synchronous with pulsation. Pulses equal, but later than heart.

CASE 10. (E. Willett, Transactions of the London Pathological Society, 1892, xliii., 38.) Descending aortic arch. Male, aged four years. Family history negative. No diseases of childhood. Slight cough for two months. Onset sudden, with malaise, headache, and hallucinations. Ascites and œdema of face and legs. Systolic murmur heard over entire cardiac area. Aneurism thought to be due to a suppurating lymph gland which discharged into the aorta. Death due to pericarditis with a bronchopneumonia.

CASE 11. (R. A. H. MacKeen, Medical News, 1892, lxi., 272.) Aortic arch. Female, aged four years and nine months. Family history negative. No diseases of childhood. Six months before fell striking breast, producing no immediate symptoms. Later a continuous hacking cough and shortness of breath. Pulsating swelling in first left intercostal space, expansile in character; slight thrill; systolic murmur; left radial pulse slowed. No aphonia. Death due to pneumonia.

CASE 12. (A. A. Smith, Medical Record, 1893, xliv., 349.) Ascending and transverse aortic arch. Male, aged eighteen years. Rheumatism one year before. Dyspnœa, extremities always cold. Marked thrill; dulness over ascending and transverse portion of aortic arch; double murmur; thrill in carotids.

CASE 13. (F. J. Smith, Transactions of the London Pathological Society, 1897, xlviii., 53.) Descending aortic arch. Male, aged nine years. Heart and vessels normal. Dyspnœa the only symptom, marked and of sudden onset. Death following tracheotomy.

CASE 14. (S. H Berry, British Medical Journal, 1898, ii., 1745.) Ascending aorta. Male, aged fifteen years. Slight thickening of the aortic valves. No history of rheumatism or syphilis; no œdema; pupils equal. Dropped dead while playing cricket. Pericardium distended with blood clot.

CASE 15. (G. Bacelli, Semaine Médical de Paris, 1898, xviii., 137.) Aortic arch. Male, aged seventeen years. Family history negative. Acute articular rheumatism at fifteen years of age. No previous illness; no dyspnœa, pain, or palpitation of heart. Six months before present time there was pain in left knee and elbow radiating from shoulders to spine, accompanied by fever. Swelling in pericardial region; thrill of maximum intensity in jugular fossæ and second right intercostal space. Two murmurs; first harsher and best heard in second right space, the second over the sternum. Left radial pulse stronger than right.

CASE 16. (I. Burn Murdock and D. A. Welsh, Edinburgh Hospital Report, 1900, vi., 84.) Ascending aorta. Male, aged twelve years. Aortic and mitral valves diseased. Heart hypertrophied. Vessels normal. Family history negative. Congenital heart disease discovered when three years old. Delicate, sallow complexion, frequent cough, fair muscular development, slight clubbing of fingers and toes, superficial veins of extremities engorged; wavy pulsation in third and fourth left interspaces, visible carotid pulsation. Rough thrill over base of heart. Cardiac dulness increased one-half inch to right of sternum. Rough systolic and diastolic murmurs heard in aortic area, over sternum, in vessels of neck and body of heart. Heart sounds obscured. Death due to ulcerative endocarditis.

CASE 17. (Author's case, 1902.) Transverse aortic arch. Female, aged nine years. Heart hypertrophied; vessels normal. Family history negative. Pertussis and rheumatism. Pain in left wrist, cough, shortness of breath on exertion, pallor, and cold extremities. Engorged superficial veins of chest, face, neck, and arms. Pulsation over cardiac region, suprasternal notch and vessels of neck. Thrill on both sides of sternum to third rib and in supraclavicular fossæ; also a distinct thrill at apex. Tracheal tug. Radial pulses small, weak, and compressible; left pulse slower and weaker. Dulness over first and second interspaces near sternum. Heart increased one-half inch to right of sternum. Loud harsh murmur over dull area, heard less distinctly throughout thorax. Systolic and presystolic mitral murmur.

b. ABDOMINAL AORTA.

CASE 18. (Dr. Miguel, Bull. Général de Thérapeutic, 1835, ix., 393.) Abdominal aorta. Male, aged fourteen years. Heart normal; aorta narrowed and friable. Indisposed for two weeks;

lumbar pains, difficulty in walking, diarrhœa, pulse weak, and prostration. Death sudden, due to rupture of aneurism.

Case 19. (Dr. Armitage, Transactions of the London Pathological Society, 1857, ix., 85.) Abdominal aorta. Female, aged seven and a half years. Heart and vessels normal. Palpitation of heart from infancy; aching in legs, knees, and wrists when erect. Heart action violent. Systolic bellows sound at mitral areas. Sudden death due to rupture of aneurism.

Case 20. (Dr. Phanomenow, Arch. für Gynäkol., 1881, xlviii., 133.) Abdominal aorta. Fœtus. Caused dystocia from its size.

Case 21. (C. F. C. Lehlbach, reported by A. Jacobi, Transactions of the American Pediatric Society, 1889, i., 227.) Abdominal aorta. Female, aged five years and three months. Heart normal. Parents died of tuberculosis. Pertussis and measles only diseases When four years old, while jumping, felt pain in right leg, which continued and caused a limp. Operation later found pus and destruction of head of femur. Death due to tubercular meningitis.

Case 22. (R. Y. Aitken, British Medical Journal, 1898, i., 1655.) Abdominal aorta. Male, aged nine years. Heart hypertrophied; atheroma of aortic arch. Had several rheumatic attacks. Complained of pain in the chest. No circulatory changes. Death due to embolism.

Case 23. (N. N. Alexejew, Dietkaja Medicina, 1898, iii., 167.) Abdominal aorta. Female, aged ten years. Vegetations on mitral valves. Pain and depression for eight weeks. Palpable pulsation under the umbilicus. Pulse in left crural artery smaller than right.

Table II.—Cases other than Aortic.

Case 24. (A. F. Voolker, Transactions of the London Pathological Society, 1893, xlv., 51.) Aortic valve. Female, aged one and a half years. No other valvular disease; some endocarditis of aortic valve. Death due to capillary bronchitis.

Case 25. (N. Pitt, Transactions of the London Pathological Society, 1893, xlv. 51.) Aortic valve. Sex not stated, aged eleven months. No endocarditis present. Death.

Case 26. (Martin, Bull. Soc. Anatomie, 1827, ii., 17.) Ductus arteriosus. Sex not stated, aged one month. Aneurism found to be the size of small nut, filled with a clot and impervious.

Case 27. (J. Hoffnung (1), quoted by A. Jacobi, reprint from Proceedings of Tenth International Medical Congress, 1891, 7.) Branch of pulmonary artery. Female, aged ten months. In the upper lobe of the left lung was found an aneurism the size of a hazelnut, containing a firm parietal thrombus. Death due to hæmoptoë.

Case 28. (F. Rasmussen (2), quoted by A. Jacobi, reprint from Proceedings of Tenth International Medical Congress, 1891, 7.) Branch of pulmonary artery. Female, "very young." A small aneurism which had ruptured was found in lung. Patient had pulmonary phthisis. Sudden death in an attack of hemorrhage.

Case 29. (F. Rasmussen, quoted by A. Jacobi, reprint from Proceedings of Tenth International Medical Congress, 1891, 8.) Branch of pulmonary artery. Male, aged three and a half years. Aneurism had ruptured into a cavity. Patient phthisical. Sudden death during hemorrhage.

Case 30. (O. Wyss (3), quoted by A. Jacobi, reprint from Proceedings of Tenth International Medical Congress, 1891, 8.) Branch of Pulmonary artery. Sex not mentioned, aged one year. During an attack of capillary bronchitis with infiltration at right apex, vomiting and coughing followed emetic, and with it a large amount of clear red blood from nose and mouth. Death immediate.

(1) E. Henoch, Vosleo. über Kinderkrankheiten, 1889, Aufl. iv., S. 412.

(2) Hosp. Tidende, xii., Nos. 11, 12.

(3) B. Gerhardt, Handb. d. Kinderh., 111 (2), S. 807.

Case 31. (J. Sykes, Philadelphia Journal of Medical and Physical Sciences, 1823, xi., 139. Carotid. Female, aged eighteen years. Fell from a horse two years before. Aneurism the size of a goose's egg. Cured by ligature above and below; not divided.

Case 32. (Kingston, Edinburgh Medical and Surgical Journal, 1842, lvii., 69.) Right carotid. Male, aged fourteen years. Heart hypertrophied, valves normal. Vessels atheromatous. Pul sation for two years. Some pain and difficult deglutition; became larger on exertion. Sudden onset of symptoms, including a right hemiplegia and aphasia. Aneurism of basilar artery also found. Death due to embolism.

Case 33. Mr. Hodgson, mentioned by T. Smith, British Medical Journal, 1867, i., 280.) Carotid. Female, aged ten years.

Case 34. (K. C. Bose, Indian Medical Gazette, 1888, xxiii., 209.) Facial. Sex not mentioned, aged one year. Traumatic origin.

Case 35. (Sir Wm. Gull, 1857, quoted by Parker, Med. Chir. Trans., 1884, lxvii., 51.) Axillary. Female, aged fourteen years. Aortic valves diseased. Vessels normal. No rheumatic or specific history. Left hemiplegia developed during sleep. Death due to cerebral hem orrhage

CASE 36. (Wm. C. Mardorf, Medical Review, St. Louis, 1898, xxxvii., 361.) Left axillary. Female, aged nine days. No thrill. Had disappeared when she was seven months of age.

CASE 37. (G. Pollock, British Medical Journal, 1886, ii., 1033.) Brachial. Male, aged fourteen years. Vegetations on the aortic valves. Aneurism first seen three days before admission to hospital. Death due to embolism.

CASE 38. (Joubert, quoted by Bramann, Arch. für klin. Chir., 1886, xxxiii., 22.) Brachial. Male, aged eighteen years. Spontaneous origin. Cured.

CASE 39. (W. W. Keen, Medical News, 1887, li., 725.) Brachial, also an aneurism in thorax. Female, aged eighteen years. Heart normal. Spontaneous origin. Above outer third of right clavicle there is a thrill and bruit; heard also over the right carotid and subclavian.

CASE 40. (Ogle, 1865, quoted by Parker, Med.-Chir. Trans., 1884, lxvii., 51.) Ulnar. Male, aged seventeen years. Mitral valves diseased. Vessels diseased. Sudden unconsciousness, aphasia, and right hemiplegia. Death.

CASE 41. (Z. Wornarski, Australian Medical Journal, May 15, 1884.) Interosseous of hand. Female, aged twelve years. Heart normal. While lifting a weight felt something give way in left hand; noticed pulsating swelling in palm. Family history negative. No rheumatism or scarlet fever. Cured by operation.

CASE 42. (W. W. Keen, Medical News, 1887, li., 725.) Interosseous of hand. Female, aged eight years. Due to strain while exercising.

CASE 43. (N. Moore, Transactions of the London Pathological Society, 1882, xxxiv., 71.) Right common iliac. Female, aged seven years. Heart hypertrophied, vegetations on aortic and mitral valves. Vessels normal. Rheumatic history. Ill for six weeks; double murmur heard at base, systolic murmur at apex; clubbing of fingers and toes. Death due to embolism.

CASE 44. (H. H. Clutton, Transactions of the London Clinical Society, 1892, xxvi., 7.) External iliac. Male, aged six years. Ligature above and below aneurism. Cured.

CASE 45. (Grundy, London Medical Gazette, 1834, xiii., 509.) Femoral. Male, aged nine years. Received a kick in thigh eighteen months before. Healthy up to that time.

CASE 46. (T. Smith, British Medical Journal, 1867, i., 280.) Common femoral. Male, aged twelve years. Aortic valves diseased. Vessels normal. Three months before while running felt a sharp pain in the right groin, followed by a pulsating mass, over which could be heard a bruit. Rough systolic murmur at base of heart. Cardiac dulness increased. Veins of chest prominent. Is said to have died some years later of internal (aortic?) aneurism.

CASE 47. (Habershon, quoted by Parker, Med.-Chir. Trans., 1884, lxvii., 51.) Femoral. Male, aged sixteen years. Aortic and mitral valves diseased. Cerebral arteries diseased. Rheumatic fever twelve months before; ulcerative endocarditis on admission. Died comatose after convulsions.

CASE 48. (R. W. Parker, Med.-Chir. Trans., 1884, lxvii., 51.) Common femoral. Male, aged twelve years and seven months. Heart hypertrophied. Aortic valves diseased. Vessels normal. Family history negative. Disease of hip-joint due to injury when two years of age. Sudden pain in left groin followed by swelling. Pale, emaciated, clubbed fingers and toes. Pulsating swelling over femoral artery. Aortic systolic and soft mitral murmurs.

CASE 49. (O. von Bungner, Arch. für klin. Chir., 1890, xl., 312.) Left femoral. Male, aged seventeen years. Mitral valve diseased. Narrowing of vessels. Attacks of polyarthritis when eight, thirteen, and sixteen years old, resulting in cardiac disease. Swelling appeared suddenly.

CASE 50. (R. Johnson, Transactions of the London Clinical Society, 1898, xxxi., 288.) Right femoral. Female, aged twelve years. Patient thin, pale, clubbed fingers. Rheumatic fever two years before, again two months before present history. Pain and lameness for nine months. Cured by operation.

CASE 51. (Syme, London and Edinburgh Monthly Journal of Medical Science, October, 1844, 823.) Popliteal. Male, aged nine years. Swelling for two years which disappeared on pressure. Caused no symptoms. Cured by tying the femoral artery.

CASE 52. (Boling, quoted by Bramann, Arch. für klin. Chir., 1886, xxxiii., 38.) Popliteal. Male, aged sixteen years. Spontaneous origin. Pain for six months; swelling back of knee. Amputation.

CASE 53. (Madrazo, Écho Médical Toulouse, 1888, ii., 93.) Popliteal. Male, aged fifteen years.

CASE 54. (A. T. Norton, British Medical Journal 1891. i., 852.) Left popliteal. Male, aged seventeen years. Pain for five months, with swelling and expansile pulsation, over which was heard a systolic bruit. Cured by operation.

CASE 55. (Terrier and Hartman, Medical Record, 1893, xliv., 237, abstracted from Lancet.) Right popliteal. Male, aged seventeen years. Sudden pain in right ham, with swelling and redness. Operation disclosed exostosis at lower end of femur, which caused rupture of artery and aneurismal formation.

CASE 56. (Sir A. Cooper, Lectures edit. Tynell, 1824, ii., 40.) Anterior tibial. Male, aged eleven years.

CASE 57. (Moulinié, Journal Hebdomod., 1832, ix., 226.) Anterior tibial. Female, aged nineteen years. Aneurism became large. Ligature of anterior tibial followed by amputation on account of hemorrhage. Death.

CASE 58. (Clive, 1824, quoted by Sir A. Cooper.) Dorsalis pedis. Male, age not given.

CASE 59. (G. M. Withe, reported by A. Jacobi, reprint from the Proceedings of the Tenth International Medical Congress, 1891, 8.) Right external iliac and femoral. Female, aged seven years. Vegetations on mitral valves, thickening of aortic valves. Narrowing of aorta. Rheumatic and gouty family history. Rheumatism when three years of age; well-marked valvular lesion. Aneurism of left femoral appeared first, followed by tumor in the right inguinal region. Death due to malignant ulcerative endocarditis.

CASE 60. (Eppinger, quoted by A. Jacobi, reprint from the Proceedings of the Tenth International Medical Congress, 1891, 6.) Multiple of the heart. Female, aged ten years. Large number of aneurisms in the heart muscle and along the walls of the coronary and intercostal arteries. Death.

In going over the literature relative to extracranial aneurism in early life, there have been noted sixty cases under twenty years of age.

The seat of the aneurism: in 18 cases, the thoracic aorta; 5 cases, the abdominal aorta; 2 cases, aortic valves; 1 case, the ductus arteriosus; 1 case, multiple aneurisms of the heart; 4 cases, in branches of the pulmonary artery. The remaining cases are distributed among the arteries which supply the extremities.

Going somewhat further into detail in regard to the aortic aneurisms, we find that sex plays an unimportant part in early life: ten cases males, eight cases females, two cases with sex not mentioned.

In regard to age, there are fourteen cases under twelve and nine cases over twelve years.

The etiology for the most part is obscure; in six cases there was no history of syphilis, rheumatism, or severe illness. Two cases in which traumatism was the cause. Two cases with sudden onset after exertion (climbing a ladder and playing cricket). Three cases with a history of rheumatism. One case thought to have been due to an abscess which ulcerated into the aorta. One case thought to have been due to a suppurating lymph gland discharging into the aorta.

The condition of the heart: in eight cases the heart is stated to have been normal; two cases of hypertrophy; one case of hypertrophy with disease of the aortic valves; one case of hypertrophy with disease of the aortic and mitral valves; three cases with diseased aortic valves; one case with diseased aortic, mitral, and tricuspid valves; one case with diseased mitral valves. There was thinning of the aortic walls in two cases, and in two others there were some atheromatous patches in the wall of the aorta.

With few exceptions the cases cited were under observation a short time only; of these, one case is thought to have existed for six years. At that time there is the history of a fall, followed by pain in the chest, which continued at intervals with no other symptoms (Case 9).

In another case there is a history of dyspnœa on exertion for five years, with successive attacks two years before she came under observation (Case 3).

A third case is one with a history of rheumatism two years before, followed a few months later by pain in the left shoulder (Case 15).

In the majority of cases death has been sudden. The causes as found have been: three cases of rupture, two cases of acute pericarditis, one case of ulcerative endocarditis, one case of embolism, and one case due to aphasia.

Few symptoms are given, dyspnœa on exertion being the most common; pain of variable intensity, cough, pallor, cyanosis, and rarely clubbing of fingers and toes, distended superficial veins, visible pulsation, and bulging over aneurism.

SOME NOTES ON THE OPIUM HABIT AND ITS TREATMENT.

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In the opening note to his *Tramping with Tramps*, Josiah Flynt writes: "During my university studies in Berlin I saw my fellow-students working in scientific laboratories to discover the minutest parasitic forms of life, and later publishing their discoveries in book form as valuable contributions to knowledge. In writing on what I have learned concerning human parasites by an experience that may be called scientific in so far as it deals with the subject on its own ground, and in its peculiar conditions and environment, I seem to myself to be doing similar work with a like purpose."

With some such similar point of view I present the following brief note on the study of some phases of the "opium habitué" in the "open."

In a recent discussion held before the New York Academy of Medicine on the subject of alcoholism, Dr. M. Allen Starr made an interesting series of comments, saying, among other things, that one is inclined, when speaking on the subject of alcoholism, to assume that inasmuch as all spirituous liquors contain alcohol, the effects are all alike. This, he emphasized, was a gratuitous assumption, and further showed that the results due to drinking different types of alcoholic liquor were very diverse if one would think of the psychological manifestations. Thus he brought out different temperamental

variations as produced by such drinks as sherry, port, champagne, and Burgundy. These differences, he said, are due, perhaps, in part at least, to the varying composition of the drink in question, and any discussion of the alcohol question should take such differences into account.

In much the same manner it is assumed by many, if not most, that the opium habit is just the opium habit, and "there 's an end on 't;" but such is far from being the case, and I know of no psychological problem that offers a more extended gamut of individual variation than this. Its developmental history, various forms, associated customs, and devious endings are extremely multiplex; and personally I hesitate to use the general term, since to my mind, at least, it offers so few tangible conceptions. Moreover, the laying down of general rules concerning its treatment, so far as my own experience is concerned, is fruitless. The habit is a complex social-psychological network, and its treatment should take into consideration the many factors that enter into it.

An interesting field for speculation concerning this habit lies in its consideration as a "social disease," viewing for the moment society as an organism, as Spencer has so interestingly done in his *Principles of Sociology*. From this outlook the study of the opium habit would legitimately take into consideration the various types of the disease or habit; the incidence or morbidity of the affection; its causative factors, under which general head particular attention should be paid to special factors—foci of infection, I believe they might very reasonably and rationally be termed. The modes of propagation are almost as definite, and the more one sees of the habitués the fewer seem the avenues along which they have travelled to arrive at the final goal of complete destruction.

Following along some such scheme as this, the ordinary manifestations of the affection would make the next legitimate subject of inquiry. On this point it is not my purpose to dilate, but I believe, from a thorough study of most of the literature of the past ten years, that many vital points have been completely misinterpreted in this affection. Most writers are prone to be influenced by their so-called moral bias, and seem to be unable to approach this question with an unprejudiced mind. This is well illustrated by the tempest in a tea-pot in our daily and medical press which arose from a recent statement of Rudyard Kipling concerning the use of opium in the Oriental countries. It is very difficult in any sociological problem to understand one's own place in one's own environment; it is, therefore, doubly difficult for a European or American to appreciate the Oriental, and, indeed, it is fruitless to discuss such far-away matters when there is plenty of food for reflection at home.

The treatment, both prophylactic and actual, would conclude the outline of a paper such as I have suggested. This, too, is extremely broad in its scope, and requires an intimate knowledge of the personality of the sick individual. To handle it in all of its phases is almost impossible apart from a monographic analysis.

Two sharply dividing lines can be drawn, however, between the sanatorium and open modes of treatment. They are very distinct, and I hope to say more about this when the subject of treatment is reached. In the present paper I have touched here and there only on the framework just outlined.

The general classification of the types of this affection may be entered on with some degree of certainty.

As far as the general grouping of the different types of habit is concerned, three main divisions appeal to my experience. Opium-takers may be classed as those who take the drug in the form of some one of its official preparations—laudanum, paregoric, the extract, etc., by the mouth, by the rectum, by the vagina, or other natural orifice; a second and very large class, if not the largest, absorb the drug through the respiratory mucous membrane by means of the pipe or by smelling; the third class includes those who take morphine or allied products by the mouth, or subcutaneously by the hypodermic syringe. New York City affords an excellent *locale* for observing the three main types of addiction mentioned.

Incidence. It is futile, at the present time, to attempt to compute the number of people who use this drug; but there can be no doubt that its habitual use is very extensive and its occasional indulgence enormous.

Without going into this question too extensively, a few side lights gathered from prison records and from the experience of those associated with the classes who are prone to this habit make it apparent, to me at least, that the frequent use of opium for purposes of pleasure is enormous and beyond computation; and that its habitual use is certainly distributed in New York City among about 30,000 individuals. These figures are founded on very meagre statistics, yet in the course of this inquiry much collateral information has been gathered which gives some support to this general statement.

Of the incidence of this habit in other places, Dr. A. P. Grinnell,[1] of Burlington, Vt., has given the profession the results of one of the few systematic inquiries regarding the prevalence of any drug habit in a limited area. He instituted a series of inquiries among the druggists and sellers of general merchandise in the State of Vermont, endeavoring to obtain an accurate account of the quantities of narcotic drugs

[1] Medico-Legal Journal, September, 1901.

sold. His returns were but fragmentary, and are by him computed as representing but one-fifth of the total sales, yet they indicate that over three million doses of opium are sold in Vermont every month; or, stated in another way, that every man and woman over the age of twenty-one years receives at least one and one-half doses (1 grain equivalent) of opium daily.

If it is shown that the 3,300,000 doses of opium are taken monthly by a population of 187,000 people—almost twenty doses a month for the entire population—it can readily be seen that this consumption is hardly the normal consumption due to its medicinal use, but must be produced by a large number of habitual takers.

This assumption almost reaches a positive demonstration in fact when it is made apparent that the figures given and dosage represent about one-fifth of the actual consumption. It is to be regretted that Dr. Grinnell could not give us some working figures as to the number of individuals using opium habitually, but this is almost an impossible task.

For some time past the subject has interested me, and I have made some endeavor to get some light on the "morbidity" or "incidence," if I may use the word, of this habit by a side light from a different source. This has been the study of the number of "patent cures" that are placed on the market. As yet my inquiries have not yielded me definite data, but they are sufficiently advanced to warrant the belief that this will make a very profitable social study, and will give definite information bearing on the prevalence of the habit. The details of the method pursued and the mode of analysis I hope to present in a later paper bearing on the subject. The present communication I consider as a preliminary survey of a very broad field which has had very few workers who have made other than purely clinical studies.

Psychology. It is not the intention at the present time to discuss at any length the psychology of this type of habit. Such a discussion would lead one into interesting and perhaps profitable paths, but a complete exposition of the mental states accompanying this habit would lead away from the main purpose of the paper. I think that the most important element in the psychological analysis is the recognition of temperamental variations; not meaning by that the crude differentials of the phrenological pseudoscientific advocates, but one based upon more elementary and radical differences—a subject which is still in an unsatisfactory condition because of insufficient analysis of normal mental activities.[1] Not every opium habitué passes through the stages as portrayed in the glowing colors of De Quincy; in fact, my own obser-

[1] See F. Paulhan. Les Caracterse. Second edition, 1902.

vation would tend to show that but a very few have the temperamental type of De Quincy, to say nothing of his literary ability, and hence do not respond in a similar manner. This is a subject, however, that requires much analysis.

I believe that the fundamental psychological factors in the opium habit closely resemble those found in other drug habits, and that the phenomena noted for the opium habit have many features in common with those noted for the alcohol habit. This is not referring at all to similarities or dissimilarities in the physiological activities of the two drugs, but rather to the conception of what feelings the taking of the drug as an entirety, apart from individual sensational variations, gives the individual, and why he is induced to continue and why it is difficult for him to stop.

It is well known that the habit of taking intoxicants is extremely ancient, and history tells that primitive peoples used the natural intoxicants that developed in their environment. The antiquity and polygenetic origin of the alcohol habit, for instance, is admitted by all students of this habit. The use of coca has a similar antiquity, if distributed over a more restricted area. The history of the use of cannabis indica and of mescal has been preserved in the most ancient of literatures, and the pleasures of the poppy have been sung by poets and preserved in literature as old as the Pyramids.

The early religious associations of antiquity that have clustered about the use of the intoxicating properties of alcohol may have had their analogues in the peoples of the East, but my information is too scanty to warrant extended conjectures along this line. Most of the drugs used by the priests or leaders in early religious sects were of the exciting type. Frenzy and delirium were the states desired; and whether the mild states of excitement induced by the use of opium were ever utilized by those engaged in the business of religion I have as yet been unable to ascertain beyond the merest references to general practices. Thus, Dawkins[1] speaks of the early cultivation of the poppy by prehistoric (neolithic) man, but if for the purpose of joy alone or for those combined with religion I am not competent to speak. Partridge[2] has given one of the best of recent summaries of this interesting topic. But passing from early times to the present, and omitting all consideration of the many functions and ceremonies that have had bound up in their past performance some use of this drug, what is it that the present-day habitué—dully oblivious, for the most part, of the folk-lore of the past and keenly seeking an oblivion from the worries of the present—what is it that the use of this agent gives him?

[1] Early Man in Britain and his Place in the Tertiary Period.

[2] Studies in the Psychology of Alcohol. American Journal of Psychology, 1900, vol. xi. pp. 328–376.

It is a well-known pharmacological fact that the stimulant narcotics are capable of affecting consciousness in two opposite ways: they either increase or diminish the intensity of the incoming stimuli, and this heightens or clouds the waves of conscious impressions. According to the evolutionary point of view adopted by Partridge in discussing the subject of alcoholism, the habitué may be regarded as one in whom the craving for intense states of consciousness is overdeveloped, or who is lacking in control, or one who, usually as a result of pain, has an abnormal craving to revert to a state of consciousness which is less intense.

It is in this latter group that the great class of opium habitués may be classed. If he has acquired the habit, so soon as distressed or painful—sometimes termed nervous—sensations commence to crowd into his consciousness, then it becomes necessary for him to attempt to revert to a state of consciousness which is less intense and more agreeable.

Much more can be said on this topic, but I must defer it until a later period. The subject of symptomatology I shall omit entirely. Its many and diverse manifestations would warrant an entire paper; still under the head of some illustrative cases I hope to bring out a few facts that I have never seen recorded even in a wide reading.

Treatment. To assume that the attempt to cure the opium habit is an *ignis fatuus*, and that if once this habit has been acquired it is something that can never be shaken off, is an idea, for medical minds at least, that should not be entertained for an instant. Such an idea, I believe, has a prophylactic and preventive influence on the laity, and an endeavor to make it as forceful as possible is distinctly justifiable. The hell of the confirmed habitué cannot be too strongly colored if by so doing one may prevent any from entering therein. But while a pessimistic attitude on the part of the physician concerning the possibility of recovery has a certain justification from the transitory character of their ministrations, still for those who see such patients for considerable periods of time and in large numbers it is not a helpful or a correct attitude.

It should constantly be remembered that there are great variations in the intensity of habits of this kind. It has already been said that there are great numbers of pleasure habitués for opium—people who take it when they like and do not when they do not; of these I have seen many, and particularly is this true of smokers. Again, there are those in whom the desire comes as does the desire of the dipsomaniac. They go on a "dope debauch," remain under the influence of the drug for a week or two weeks, are sick, and then do not touch it again for a month, a year, or, as in one of my patients, three years; and yet this patient was a steady smoker from the age of sixteen to twenty-five years, and gave it up on moving to another city. On returning to New

York, as he does at infrequent intervals—six months, one year, or two years—he hunts up his old-time associates and has a session as in days of yore.

Cases are numerous in which the patient has voluntarily given up the drug and has never taken it again. This I know to be true of those addicted to all types of the habit—crude drug or its preparations, pipe, and even the "gun" or hypodermic. In the literature numerous instances are recorded. One of the most recent and striking is reported by W. E. Taylor:[1]

"The case reported is that of a laborer who had been using from 20 to 30 grains of opium daily for sixteen years, and who, without medical assistance or any encouragement whatever, broke off the habit suddenly, notwithstanding severe pain, insomnia, and other physical distress lasting for six weeks. At the end of three months he was perfectly cured, and at the end of nine months had not taken opium in any form, and did not crave it."

Histories of this kind are very frequent, I believe; but it is difficult to obtain them, because the former habitué recognizes the imperfections of society, with its lack of sympathy for many of its members, and the all-too-ready tendency of certain individuals to grasp an opportunity to injure another if good to self can come thereby in actuality or even in hope; and thus he hesitates to let even his friends know of this dark chapter of his life, because of their lack of comprehension of what it really means and their tendency to avoid him in the future. When it is remembered how pessimistic many are regarding the cure of this affection, reticence is by far the wisest course, else perhaps his friends will still believe that he practises the habit, and will trim their social sails to this wind of interpretation; and every alienist knows how simple it is to see insane actions in isolated happenings if once the idea has arisen that such an interpretation is possible.

The type of steady smoker of whom I have already spoken, for the most part, does not desire to get over his habit. He is able to attend to business—a banker, broker, actor, vaudeville performer, drummer, confidence man, gambler, race-track attendant, or bum, for thus the gamut runs; he is able to do his routine work, and spends his hour or two in the pleasures of the poppy every day or every other day, as the case may be. For a number of years he continues this, and does not suffer to any great extent. When sudden intercurrent disease comes, the strain tells, and pneumonia, typhoid, dysentery, gastritis, prove fatal with apparently greater frequency than among those non-habituated. This, I think, is particularly true of habitués who suffer from gastric and intestinal disturbances.

[1] Journal of the American Medical Association, June 22, 1901.

Very frequently, however, some slight intercurrent trouble throws these patients out of their stride, and it is interesting to see with what regularity they commence to take some type of "cure." They rarely consult a physician—unless a broken-down fiction of one, himself a helpless slave—in this early fright, but almost invariably fly to one of the patent specifics, of which there are legion, and concerning the claims of which I hope to be able at some future time to present a complete analysis—a subject which has been of interest ever since an appreciation of the extent and the scope of the patent-medicine business began to dawn upon me.

Many of these patients recover during these spasmodic reforms, and recover by means of the patent medicines. This I know to be a truth. But for those who would consult the general practitioner, seeking something better than the oft-repeated counsels of their fellow-sufferers, what advice can we offer which will appear rational to one who has tried countless specifics and sought advice from numerous sources?

It is here that the sharp line must be drawn between the sanitarium and the outside patient. In the former instance let the physician in charge of the sanitarium worry about the case. With him almost any mode of procedure is going to result in a temporary cure at least. For the man or woman who earnestly desires to overcome a habit, and yet is to be permitted to attend to business or the avocations of society, the problem is much more difficult of solution, if not at times impossible.

The cardinal principles on which a rational therapy are to be founded consist, I believe, in the substitution of different ideas by suggestion and the substitution of different sensations by other drugs. These two factors, if judiciously combined, will certainly be of service in the most intractable cases.

It is necessary in the first place, however, to obtain some relief from the actual sufferings of the morphinomaniac before one can use mental influences, and therefore the principle of substituted sensations must first be brought into play.

Many drugs have been employed to bring about this purpose, but practically none have been of service outside of sanitaria or in patients confined to rooms and under surveillance. For such my own experience confirms that of many others, that the bromide method is one of the very best. This method, of late years, has been termed the Macleod method, but as an actual fact the use of bromides is much older—how old no one can now say. The details of this method are as follows: 120 grains of sodium bromide are given in half a tumbler of water, every two hours during the daytime, until 1 ounce has been administered in the same day. This may be sufficient to produce the "bromide sleep," or the drug may have to be continued on the third day. It is a safe rule to stop the administration after twenty-four

hours if the drowsiness is so profound that the patient cannot be aroused from sleep to take further doses, or when aroused is incoherent, since it is to be remembered that the drug acts in a cumulative manner. After the second or third day of the sleep, which may even deepen into coma, the bromide is withdrawn. There is usually some difficulty in feeding the patient, swallowing being sometimes impossible, so that rectal alimentation has to be practised; and a tendency to aspiration pneumonia, which occasionally manifests itself, makes feeding by the mouth doubly dangerous.

This plan of treatment was, it seems, discovered accidentally. Macleod states that early in 1897 a neurasthenic woman, who had been addicted to morphine for nine years, by accident received doses of over $2\frac{1}{2}$ ounces of sodium bromide in a little over two days. A profound sleep was induced, lasting several days, and when its effect wore off the craving for morphine had ceased, and with it the various disturbances which had led to its use.

Any septic condition of the pharynx or of the nasopharynx or the mouth should contraindicate the method, and a weak heart or impaired pulmonary conditions are to be regarded as strong contraindications. It has been suggested that sodium bromide in large quantities has a distinctly harmful effect upon the kidneys, and therefore any degree of nephritis is to be regarded as a barrier to the "bromide sleep."

Although the bromide plan of treatment is far from being simple and unattended by danger, yet compared with the dangers attending the ordinary treatment for the morphine habit it seems to be of marked value in well-selected cases, and in such the writer would not hesitate, under appropriate safeguards, to employ it.

Of the use of hyoscine in comparatively large doses, as advocated by many on the introduction of this drug, and recently commended by Drs. Lott and Hare, my own experience is contradictory. It has proven of good service in stages of marked excitement, but its use has given me more than one unpleasant shock in that dangerous collapse has followed its administration.

Inasmuch as the chemistry of this group of alkaloids is in a most unsatisfactory state of uncertainty, very few of them being pure products, hyoscine should be pushed with much caution.

While being the last one to hold forward a single remedy for the treatment of such a complex condition, it seems that if once one is enabled to relieve the habitué of the sense of ennui and unrest that afflicts him at the recurrence of his dosage time—be it once in six hours, or twelve, or every day or two, as the case may be—then with the relief given at such a time by other means than by morphine a point is reached where other means of influencing the patient are more liable to be of effect, both temporary and lasting.

Much has been claimed of the newer morphine modifications—heroin, dionin, and peronin—within the past few years as fulfilling this very indication. From a somewhat extended use of these remedies I believe this to be in part true; but they are by no means as efficient as many have been led to believe, as I think, from too hasty a recital of the results. In the earliest days of my experience with these drugs the belief was engendered that Eldorado had been found; but after waiting three to six months it became apparent that in some cases I had simply substituted one habit for the other, and it is still an open question as to which is the more desirable one.

Many observations have been made on the use of these remedies. The most valuable by far is that of Morel Lavallée,[1] who treats of heroin alone. He brings out, in sharper contrast than is warranted in my own experience, differences in the use of morphine and heroin. Thus if to a healthy man a hypodermic injection of morphine be administered the effects that follow are, as is fairly well appreciated, a blissful feeling of tranquillity accompanied by a sharpening of the intellectual faculties. All anxieties are forgotten in the pleasure of simply living. As far as the habitué is concerned, he feels his strength and his usual vigor return; all his lassitude disappears. The non-habituated man feels his whole body thrill with a pleasant glow that seems to run through his blood. His pulse is quickened and his respiration diminished. It is chiefly this sense of living warmth which is the secret charm of the physiological effect of morphine, and which is called "euphoria." There is also a physical sense of pleasure in living, akin to the psychical content.

Under the use of heroin practically all of the sensations observed in the use of morphine are duplicated, but to a minor degree. There are, however, if the experiences related to me are to be accounted at all trustworthy, certain points of difference. Whether such arise in the early period of the use of heroin alone or are observable throughout, it is yet too early to say, although I am inclined to believe that later the differences in subjective variations are inappreciable.

Under heroin the sense of euphoria is not an exaltation of the cerebral functions, neither is it a forgetfulness of all external impressions, nor yet the joy of living in a world apart from this real world: it seems to be simply the loss of desire, a cessation of "craving;" and if the patient has been previously addicted to the use of morphine, heroin induces a physiological equivalent in giving contentment. To the healthy man the sensations of pleasure are not wanting. There may be marked relief from pain, but the delicious sense of pleasurable warmth and comfort that steals over the body is lacking to the same

[1] Revue de Médecine, October and November, 1900.

degree. The sense of coldness disappears, and the hot flashes observed with morphine may also be present; but it does not seem to be that vague glow that can in a moment revive a weak body and give it a new feeling of vigor. The sense of weakness experienced by the habitué does disappear, but it is imperceptible. I have not been able to obtain a history of the sudden access of mental and physical vigor that so often follows the use of morphine by the habitué, although some patients have said that heroin "has morphine skinned to death."

Lavallée states that but few individuals experience euphoria from heroin. My own experience is not so. Most have felt it, and even when given by the mouth—a distinct point of difference in the observations of Lavallée and my own. In one patient I can well remember that she was almost impressionless to any amount of morphine, being a "grand morphinomaniac," as the French call them, taking indifferently from 20 to 50 grains a day hypodermically, yet ½ grain of heroin give her distinct euphoria—a new sensation, which she was loud in proclaiming had not been her joy for many years. For a time it seemed that I might be able to help her habit, but unfortunate domestic ties made former associationship inevitable, and she has disappeared from observation.

Observations. A few illustrative cases are here reported, some of which are distinctly out of the ordinary run. They are offered as fuel to the social as well as to the medical grist. These cases have been chosen more as types than as individuals. They illustrate failures as well as successes, and also show some of the factors which militate against the probability of cure in some instances.

Report of Cases.

Case I.—H. M., aged thirty years; occupation, green-goods man. His early history is of interest. His father and mother were working-class people living in the crowded tenement-house districts of lower New York City. He went to public school, and at the age of fourteen or fifteen years obtained a position as lookout at the door of an opium joint. He soon learned how to smoke, and at the age of sixteen years was a confirmed smoker. He was an attendant in the joint for a couple of years, and then went on the vaudeville stage, doing a song-and-dance turn. He continued in this line for three or four years, but the work became too hard for him, and he drifted into the line of bunco-steering, at which he is said to have been a clever artist. He began using the syringe at this time, at first using 2 to 3 grains of morphine a day. For the past five or six years this dose has been increasing, so that at one time his average daily quantity varied from 60 to 90 grains. One day he took ½ ounce—120 grains. He invariably took his solution hot, heating a teaspoonful of water over an alcohol lamp and placing a cube of 4 to 5 grains at one time in the spoon. This was injected while still hot—just below the point of actual burning. In this manner he was able to get larger doses and thus obtain

a more continued action, as he explained, since large quantities of the drug were thrown out of solution beneath the skin, because the normal body heat reduced the temperature. It is very improbable that any differentiation of sensation could be experienced by the patient between doses over 60 grains a day; but there is no doubt, in my mind at least, that when doses of less than 60 grains were taken distinct sensations of distress could be appreciated.

When this patient came under treatment he was in a very bad condition. Sleep, even with enormous doses, was almost impossible. His appetite was very capricious, and rectal and bladder power were lost. Continued *fellatio* gave sexual satisfaction.

In treating him the psychical element of companionship seemed to be one of the strongest aids. Of his own accord, and with full liberty, he gradually diminished the dose to 15, 10, 8, 7, 6, 5, 4, 3, 2 grains a day, reaching a stage varying from 4 to 2 grains a day in about four weeks. At this point his suffering was very extreme, and an infinite amount of patience, tact, and ingenuity in devising lines of thought and inquiry were necessary to keep him at all contented. He was held on this dose for about two weeks, and had begun to gain control of himself, when an unfortunate family episode upset his self-control and resulted in a tragedy.

His greatest boast and pride had been that he was gradually conquering the hold of the drug for the sake of his wife and his home; and this psychical stimulus, although at best but a very sentimental one, was pushed to its fullest extent in the course of the treatment; and when he found, on coming home at an unexpected hour, his wife and her paramour in a compromising position, his already overtaxed nervous system gave way, and he promptly drew a pistol, shot at the retreating marauder, shot his wife non-fatally through the shoulder, and then placed the end of the barrel in his mouth and killed himself.

This case needs no comment. Its dramatic ending gives an inkling of the extreme state of mental unrest that was this patient's. Had this accident not occurred I believe it was possible and probable that the provisional cure of the patient might have resulted.

A somewhat similar case occurring in a man of somewhat higher social status resulted in a cure by the same methods.

By method—it might almost seem lack of method, it being only by the power of forceful and repeated suggestion—these patients were enabled to reduce the dosage of their own volition. I believe that for this class of ambulatory cases—those not confined to an institution—almost the only step that promises hope is that of implicit confidence in the patient and a mutual trust. If the patient backslides and confesses it, there is some hope that his confidence is being gained and that the remnant of self-respect is being kept alive. For these patients I insist that they keep a note-book of just how much morphine they take, recording the amount and the hour and minute it was taken, and what differences were to be noted in the sensations as the doses are being reduced. They are permitted the use of their own syringe, and the only obligation is that they take so much and record it.

It may seem trivial to record these observations, and the pessimist may greet them with a smile of incredulity; nothing is more natural, and similar doubts were aroused in my own mind, when an habitué—in fact, several—told me that the only reason why they never had any success in getting cured was that they were not trusted and permitted to do as they themselves wished. That they must work out their own salvation with fear and trembling is, I believe, a primary canon.

Case II.—H. S., aged thirty-nine years. This patient learned to smoke at the age of seventeen years, having been taught by an actress. For a short time he worked about a theatre in New York, and then went as an assistant to a tight-rope walker. Many ups and downs have occurred in his life, but for seventeen years at least he had smoked the pipe. About four years ago he came under my care, and in about one year a cure was effected. This patient is an accomplished cooker of opium pills, and can lie around a layout for hours, but has had no desire to touch the pipe during this interval of time. It is of interest to note that $\frac{1}{6}$ grain of heroin or of dionin gives this patient a sense of euphoria which, in his own vernacular, "has the pipe skinned to death."

Case III.—This third patient, D. W., aged fifty-one years, serves as a type of a number, a half-score of whom I have seen within the past year. He represents what may be called the substituted habitué, and is typical of what happens to those who pursue the downward path which has but one ending. Beginning as a smoker, he gradually acquired the morphine habit, first by inhalation in cigarettes, then taking it by the mouth, then by the hypodermic. About two years ago he came under treatment by one of the newer morphine derivatives. In the early months of his treatment it seemed that success was to be achieved, but he soon so thoroughly enjoyed his new substitute that he finally found out what it was, and is now a confirmed habitué of this newer morphine derivative.

Whereas for the laity I believe that this history is an exception, for opium habitués and for those who know of the newer drugs it will be inevitable that some will take them up for the simple reason that they provide a different stimulus and a new one.

Case IV.—C. W., a native of Pennsylvania—a woman, aged twenty-six years—affords an extremely interesting illustration of medico-legal import. This patient was of the periodical type. She would leave her home about twice a year, would come to New York, and for two months go on a debauch in which she drank and smoked opium, took morphine by the mouth, and frequented the Tenderloin both for pleasure and profit, although a woman in a comparatively upper walk in life.

After several years she became accustomed to the use of opium, and finally came to take morphine regularly by the mouth. The reason for her coming under medical observation was peculiar. She obtained a prescription for ten $\frac{1}{4}$-grain morphine sulphate tablets from a young and unsuspecting practitioner, altered his figures to read one hundred, and obtained from the druggist this number; but the pharmacist gave

her one hundred ¼-grain morphine tablets with $\frac{1}{200}$ grain atropine, and when she promptly swallowed ten she came under observation suffering from severe atropine poisoning.

This patient made a recovery from the poisoning, and under treatment for the morphinism has gone back to the pipe. This means one step in the cure of many patients, although it is true that most go the other way. In fact, among smokers it is often regarded that when one goes from the pipe to the "gun" they are going down hill.

VOLVULUS OF THE SMALL INTESTINE—ITS RELATIONS TO HERNIA. TORSION OF THE ENTIRE MESENTERY. REPORT AND RÉSUMÉ OF CASES.[1]

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Some years ago Leichtenstern found in about 1500 cases of intestinal obstruction that only 33, or a little over 2 per cent., were caused by volvulus.

In Gibson's recent article—"A Study of 1000 Operations for Acute Intestinal Obstruction and Gangrenous Hernia"—volvulus is given as the cause of obstruction in 12 per cent. of the cases, becoming fourth in the list of causes, hernia holding the first place, with 35 per cent., and intussusception and bands becoming second and third, each occurring in about 19 per cent. of cases; so volvulus is now recognized far more frequently than formerly as a cause of intestinal obstruction.

Definition. Volvulus is from the Latin word *volvere*, to roll. In surgery it means the rolling or turning of the intestine and mesentery in such a manner as to obstruct the lumen of the intestine, the circulation in the bloodvessels, or both.

For a long time volvulus was used synonymously with ileus, and meant almost any form of intestinal obstruction. In a thesis written in 1765, Grol states that volvulus is caused by erysipelas, inflammation, tumors, scirrhus, fecal impaction, enteroliths, worms, and intussusception.

Early in the last century Rokitansky described three forms of volvulus:

1. Rotation of the bowel on its own axis.
2. Rotation of a loop of bowel around its mesenteric axis.
3. The intertwining of two adjacent loops of bowel.

[1] Read by title at the meeting of the Association of Military Surgeons, at Washington, D. C., June 7, 1902.

Anatomy, Etiology, and Pathology. The mesentery is a fan-shaped double fold of peritoneum extending from the vertebral column to the convolutions of the jejunum and ileum, which it envelops, forming their peritoneal coat. The root of the mesentery is about six inches broad, extending obliquely from the left side of the second lumbar vertebra to the right sacro-iliac symphysis. Its length is about four inches from the vertebral attachment to the intestines, where it spreads out like a fan to include some nineteen feet of intestine. It contains between its folds the vessels and nerves of the small intestine. The shape of the mesentery, with its narrow pedicle or root and its broad periphery, would seem to make it an easy victim of rotation whenever the vermicular motion of the intestines attached to its broad end becomes unusually active, and the only surprise is that torsion of the mesentery is not more frequent. A *portion* of the mesentery may be involved, as in case of rotation of a coil of intestine, say fifteen inches long, the portion attached to that coil would undergo torsion; or the *entire* mesentery attached to nineteen feet of intestine may be twisted by rotation around its own axis, either from right to left or from left to right, making from half a turn (180 degrees) to two complete turns, as in a case reported by Delore, in which almost the entire ileum was twisted twice around its mesentery from right to left. Bassinot believes that the direction of rotation is more frequently from right to left, as the hands of a watch move; and this opinion seems plausible when we consider the oblique attachment of the root of the mesentery, the upper border bearing to the left and the lower border to the right, so that a weight or traction acting vertically on the upper border in line with the long axis of the body when erect would tend to pull it down on the left side while the lower border ascends. This motion continued would cause rotation from right to left, or as the hands of a clock move. But my statistics, while not numerous enough to be of much value, do not sustain this theory, as in 14 cases of torsion of the entire mesentery in which the direction was given, only 6 were from right to left and 8 were in the reverse direction. Taking all the cases together of torsion of the *entire* mesentery and of *parts* of the mesentery in which the direction of the turn is given, we have 24 cases, in 11 of which the direction is from right to left and in 13 the reverse.

Rotation of a segment of intestine on its longitudinal axis is rare, but it may be caused by bands, adhesions, or tumors. A tumor attached to the upper border of a horizontal portion of intestine would by gravity tend to fall below, bringing the upper border with it, rotating the tube on its axis, and possibly diminishing its lumen and obstructing its vessels. It is more common for a tumor to produce rotation of the mesentery, as in Case 4, Series II., reported by Briddon.

Volvulus may produce obstruction of the circulation or of the lumen

of the intestine; usually it does both. Torsion of the mesentery on its axis not only arrests the venous return from the intestines—which in turn reacts on the capillary and arterial circulation, causing, if complete, rapid death of nearly the entire small bowel, often preceded by hemorrhage both into the lumen of the bowel and into the peritoneal cavity; but usually by pressure of one or both of its tightly stretched borders it obstructs the lumen of the gut, and while this *may* block both ends of the tube it almost invariably affects the lower end, usually the ileum. Sometimes the pressure is so great as to cause ulceration at the point of pressure, or division of the coats of the bowel, as was stated by Captain Smyth in Case 7, Series II.

The lumen of the intestine may be occluded by pressure of one segment of bowel on another without materially affecting the mesentery. Probably many cases of "colic" are caused by the latter form of volvulus, and as the intestine rights itself the symptoms disappear.

All authorities agree that volvulus occurs much more frequently in the colon than in the small intestine. Of 121 cases cited by Gibson 73 were in the colon, 58 in the sigmoid flexure, and 15 in other parts of the colon; and only 36, less than one-third, were found in the small intestine. Leichtenstern found in 76 cases of volvulus, 45 in the sigmoid flexure, 23 in the ileum, and 8 in the jejunum and ileum combined. In my collection no cases of volvulus of the large intestine are included.

The causes commonly given are, first, *age*. The average age of Gibson's 121 cases—both large and small intestine—was forty-five years. In my list of 54 cases—small intestine only—the average age was forty-one years, and the greatest in any decade was 11, between fifty and sixty years. If we compare the average age of the cases in which hernia was associated with volvulus with those in which there was no hernia we are at once struck with the difference, in the former the average age being fifty-four years and in the latter thirty-six years. Volvulus may occur at any age—several have been reported in persons over seventy years; and Tissier and Mercier report a congenital case.

Second, *sex*. It seems to be somewhat more frequent in males. Gibson gives 67 males to 40 females, while the proportion in my list is 32 males to 27 females.

Third, *abnormally long mesentery*. A long mesentery, like the elongated pedicle of a tumor, predisposes to rotation. The mesentery may be congenitally long, or its length may be increased by traction on the bowels by means of fecal accumulations which especially affect the sigmoid flexure, adhesions, tumors, hernia, or general loss of flesh. There is no doubt that volvulus of the mesentery proper may and does occur without elongation. With the mesentery elongated like a

pedicle, a slight force may cause the intestines to revolve and twist the mesentery on its axis. This force may be violent exercise, unusual peristaltic action as a result of indigestion, or traumatism, as in cases reported by Turner, Hawkins, Staveley, and Giddings.

Hernia is not infrequently associated with and is the cause of volvulus. Volvulus may affect the intestine and the small portion of mesentery in a hernia sac, or it may be wholly within the abdominal cavity and involve the entire mesentery, while only a short coil of intestine is found in an external hernia. Volvulus may be caused by traction of a coil of intestine attached to the highest part of the mesentery dragging it down so that it becomes the lowest part, and thus makes a half revolution (180 degrees) on its axis. Such seems to have been the condition in the following case:

CASE 21. *Volvulus with hernia; death in less than twenty-four hours.* —H. W., negro, aged thirty-five years; was taken sick January 21, 1902, at night, with pain, cramps in the bowels, and vomiting. He had had a right inguinal hernia several years, and this had come down, and he thought the trouble was caused by it, as he could not reduce it. Next morning he went to work as a laborer, but felt so weak on account of the pain in the bowels and vomiting that he had to stop, and was brought to the Emergency Hospital about 12 o'clock, January 22d. A hernia in the right side of the scrotum was reduced by taxis without difficulty, and he experienced some relief; but soon after it was noticed that his pulse had not improved—it was 100 and very weak and thready, scarcely perceptible at the wrist—and he continued to vomit. When I saw him at 4 P.M., about twenty hours after he was taken sick, he was in collapse; pulse as given; temperature subnormal (97.4° F.); voice so weak that it could scarcely be heard; little pain, but that was in the bowels. He began to vomit while I was looking at him, and vomited over 1000 c.c. of chylous-looking fluid, and immediately died.

Post-mortem Examination. On opening the abdomen over 1000 c.c. of dark, bloody fluid were found in the peritoneal cavity. The intestines which presented were black and leathery and offensive. The bulk of the gangrenous intestines lay on the left side. Examination showed a twist of the mesentery from right to left through an arc of 180 degrees, including the superior mesenteric artery and vein. The vein contained large thrombi, and the edge of the mesentery compressed a point in the small intestine about eight feet from the pylorus, enough to leave an indentation. The cæcum with appendix were drawn tightly on the stretch toward the left side, and both were gangrenous. The small intestine from the point indented by the edge of the mesentery to a point just above the cæcum, a little over thirteen feet, was gangrenous, black, and leathery. No perforation was found. The rest of the intestine above and below was in good condition, only considerably congested. The intestine contained a quantity of bloody fluid similar to that in the peritoneal cavity. It is possible that the hernia, which was a coil of the upper ileum or jejunum, started the mesentery to rotating by traction.

Sometimes the volvulus in the abdomen is kept in twist by the fixation of the coil in the hernial sac. Such was the explanation of several cases, especially those reported by Knaggs.

Symptoms and Diagnosis. The symptoms of volvulus of the small intestine are those of acute intestinal obstruction, coming on suddenly, often when the patient is seemingly in perfect health. Pain of a severe, colicky character, usually in the abdomen, although in one case it was most severe in the back (see Case 7); vomiting; rapid, feeble pulse; subnormal temperature; obstinate constipation, purgatives having no effect; distention of the abdomen, and great prostration. Vomiting is usually present, but in the histories given it was reported absent in five cases—8 per cent. Many times the vomitus becomes stercoraceous, proving that although the intestine may be obstructed below it may yet remain pervious above. The pulse may be little changed for the first six or eight hours; after that it becomes feeble, thready, and 100 to 160 a minute. The temperature is unreliable; it may be normal for a while, then somewhat elevated—100° to 101° F.; but later it is often subnormal. The abdomen is usually distended and tympanitic. In the early stages, before tympanites becomes general, a circumscribed area of tympanites in the hypogastric region, due to distention with gas of the portion of intestine involved, is a valuable symptom. There is usually tenderness over certain parts of the abdomen, and sometimes a swelling, band, or ridge can be made out by palpation. Occasionally a definite mass or tumor can be felt within the abdomen.

Rectal or vaginal examination will sometimes disclose a boggy mass in the rectovesical or rectovaginal pouch. This point has been emphasized by Major Williams, of the Indian Medical Service (Case 20), and mentioned by Homans, Littlewood, and others. While a bloody effusion often occurs both in the peritoneal cavity and in the intestine affected, blood is seldom vomited or passed at stool.

The diagnosis may be difficult as to volvulus, but it is easy to determine the existence of intestinal obstruction, and that is enough to indicate the proper line of treatment.

The most unfortunate mistakes are liable to be made when an unseen volvulus is associated with a visible hernia. A patient with hernia may have symptoms of obstruction or strangulation. The hernial sac is opened and a congested coil of intestine is reduced; but if a volvulus exists in the abdomen, as it too often does, the symptoms are not removed, and death relieves the patient unless the surgeon does by another operation. My case is a good example of this, in which the patient's life was saved by a stroke of good luck.

Case 39. *Inguinal hernia with volvulus in the abdomen; resection of intestine; recovery.*—W. G., aged sixty years; male negro; had had a right inguinal hernia for many years, and was operated on for strangu-

lation ten years ago. January 8, 1900, at 10.30 A.M., while lifting a cake of ice, the hernia came down in spite of his truss, and he was unable to reduce it. He had severe pain in the abdomen and vomiting. Patient was operated on at the Emergency Hospital at 3 P.M., four and a half hours after the symptoms began, under chloroform. The tumor was about the size of an adult head, and very tense and dull on percussion over the lower part. The sac, which was anatomically congenital, was opened and found to contain the cæcum, part of the ileum, and a large mass of omentum, which was adherent to the bottom of the sac. The small intestine was slightly congested and was reduced, when, to my surprise, a coil of small intestine, black and gangrenous, came into view. It was up to this moment in the abdominal cavity and not in the hernial sac. The coil was pulled down until a sound part was reached, and twenty-eight inches were resected and the ends united with a Murphy button. The mesentery was swollen and œdematous. The omentum was ligated, cut away from the sac, and returned to the abdominal cavity, and Bassini's operation for the radical cure of hernia was performed, the wound being closed without drainage. The patient recovered without incident, passing the Murphy button on the fourteenth day, and was discharged on the eighteenth day after the operation. When seen more than a year later, he was perfectly well.

PROGNOSIS. In my list of 61 cases there were 51 operations, with 21 recoveries—a mortality of 60 per cent. Separating the two classes, we find 17 operations for twisting of the entire mesentery, with only 4 recoveries—a mortality of 76 per cent. Delbet's second case, which died of pneumonia eleven days after the operation, is included in the fatal cases, although in a sense it may be regarded as a success, as the patient died from another cause than the operation. There were 34 operations for volvulus of *part* of the mesentery, with 17 recoveries—a mortality of 50 per cent. Gibson reports 36 cases of volvulus of the *small* intestine operated on, with 25 deaths—a mortality of 70 per cent.; and of the colon, 73 cases, with 34 deaths—a mortality of 50 per cent. The high mortality in the operations for volvulus *entire* is due to three causes: First, *the more serious nature* of a condition which strangulates almost the entire small intestine, injures the sympathetic plexus, and perhaps produces a rapidly fatal toxæmia —less than twenty-four hours in my case; second, *delay in operating*: of the 14 cases in which the time was given which elapsed between the onset of the symptoms and the operation it ranged from ten hours to nine days, all the successful cases being operated on in less than forty-eight hours, except Major Brown's case, in which the symptoms were at first not acute; and, third, the *difficulty of recognizing the true condition*, in order to act intelligently—four operators candidly confessed their inability to do so after opening the abdomen, and the patients died without relief, the true condition being at last disclosed by a necropsy.

Treatment. G. H. Hunter advises the treatment of volvulus by rotation of the body of the patient around its long axis in the opposite direction to the volvulus, ascertaining this by the lack of pain when the patient turns in the proper direction. With the symptoms of acute obstruction usually seen in volvulus there should be no hesitation in performing laparotomy at the earliest possible moment. The abdomen should be opened near the median line, as a rule, through the right rectus muscle, in order to be more convenient to the root of the mesentery for the purpose of making an examination, unless there is a tumor perceptible, when it is best to make the incision over the tumor.

The escape of bloody fluid on opening the peritoneum is often seen. The intestines are usually distended, congested, and often brown or black in color. Examination of the coats of the intestines and the mesentery shows enlarged, swollen veins. Search should be made for other causes of obstruction—such as hernia, tumors, intussusception, bands—and then the mesentery should be examined thoroughly, removing, if necessary, all the coils of the small intestine from the abdomen in order to do so. The difficulty in finding the trouble can be better appreciated by reading the experience of Major Debrie and of Kirmisson, Delbet, and Delore. Kirmisson frankly confesses that he took the twist of the mesentery for the ligament of Treitz, and did not recognize the true condition. Delbet failed to recognize the condition in his first case, and was under the impression that it might be a retroperitoneal hernia, as two segments of intestine—one collapsed, the other distended—passed behind a tense fold of peritoneum. He made an anastomosis between these two parts of the bowel, and found at the necropsy that he had united the first part of the jejunum with the last coil of the ileum.

If the intestine is gangrenous it should be removed and an end-to-end anastomosis made unless the extent exceed ten feet; excision of a greater length, as shown by experiment and experience, is almost inevitably fatal. Gibson stated in 1900 that there was only one record of successful resection of the small intestine for volvulus—that of 127 centimetres (4⅓ feet) by Riedel. In my list of 51 operations there were 3 resections, with recovery. In one of them—Dreesman's case—2.15 metres (7 feet) were removed.

In operating on hernia with symptoms of obstruction the surgeon should always bear in mind the possibility of the existence of volvulus in the abdomen. The condition and relation of the contents of the hernial sac—as a swollen and congested loop of bowel, with insufficient constriction at the rings to account for it, or an intestine of unusual appearance which could not explain the symptoms of obstruction—should excite suspicion of this complication. In every case the sur-

geon should satisfy himself on this point by pulling down the coils of intestine, or, if necessary, by opening the abdomen.

The contents of every case of strangulated hernia should be carefully inspected—that is, under no circumstances should a *strangulated* hernia be reduced by the blind method of taxis unless there are good reasons for not operating.

Following is an abstract of 61 cases—by no means a complete list—taken from the literature. This list is divided into two classes: I. Those termed "entire"—21 in number—in which the *entire* mesentery is twisted, affecting almost the whole of the small intestine; and II., those termed "in part"—40 in number—in which only a *portion* of the mesentery is involved, and therefore only a small portion of the intestine is affected.

I. Volvulus of the Entire Mesentery.

Case 1. *Volvulus of the entire mesentery; death.*—H. Rokitansky, in 1837, reported a case of hernia complicated with volvulus in a woman, aged seventy-one years. She was admitted to the hospital in December, 1830, with symptoms of strangulated hernia. The hernia was reduced by taxis, but the patient died ten days later.

Necropsy. There was peritonitis and the mesentery folded and completely twisted on itself, forming a kind of axis 4½ inches long and 1½ inches thick, around which the small intestines were rolled. The small intestine descended from the duodenum to the right iliac fossa and twisted upon itself in front of the vertebral column, making two circuits around the axis formed by the mesentery. The intestine was discolored, soft, friable, and perforated about two inches from the ileo-cæcal valve.

Case 2 (Rokitansky). *Death.*—A woman, aged seventy-two years, in 1833, suffered with fever, nausea, pain, and tympanites of the stomach; fecal vomiting and death in three days.

Necropsy. Peritonitis. Very long mesentery, which was twisted one and a half times around its axis, the ileum occupying the upper part of the abdomen, while the jejunum occupied the left umbilical region. The species of cord formed by the mesentery (twisted) pressed the two extremities of the small intestine against the left side of the vertebral column—the ileum, which from one and a half feet from the cæcum extended downward and toward the right side, while the upper part of the jejunum passed under the mesentery in an opposite direction—upward and from right to left. Intestine deeply indented, as if cut by a ligature where pressed by the mesentery. Gangrene.

Case 3 (Rokitansky). *Death.*—A woman, aged seventy-two years, died in 1839 after suffering from abdominal pain and fecal vomiting.

Necropsy. Stomach and intestine distended with gas and yellowish liquid. The mesentery was very much elongated, and twisted on itself in such a way that the ileum was situated in the upper and the jejunum in the lower part of the abdomen, the mass of intestines occupying the left and middle region of the abdomen.

Case 4 (Rokitansky). *Death.*—A woman, aged seventy-one years, who had suffered twelve years with femoral hernia, died in 1839 from internal strangulation.

Necropsy. Distended abdomen; intestine containing gas and yellowish liquid; peritonitis. Mesentery attached to ileum was very long and folded and twisted on itself, forming an axis 4½ inches long and 1½ inches thick, around which the small intestine was wound.

Case 5. *Operation; death.*—In September, 1885, Major Mignon, of the French army, saw a man, aged twenty-eight years, who had been taken suddenly ill with vomiting and severe pain in the abdomen. These symptoms continued during the night, and he was sent to the Val du Grace Hospital next day with the diagnosis of peritonitis. Twenty-four hours after the symptoms began the patient was hollow-eyed, with cold extremities; pulse 150, and feeble; temperature, 39° C.; abdomen distended only in the lower half; nausea and vomiting. Frequent desire to go to stool, but without effect. Laparotomy about thirty-six hours after the onset of the trouble, giving exit to 1500 c.c. of yellow fluid; the intestines were distended and purple. The mesentery of the small intestine was found twisted once on itself from *left* to *right* and from below upward, making a cord about one inch thick. This was untwisted, and the patient passed 200 grammes of liquid fecal matter, but died five hours after operation.

Case 6. *Operation; recovery.*—Routier's case is as follows: A woman was taken suddenly ill in the night of January 8, 1890, with severe pain in the region of the transverse colon. Next day, the 9th, vomiting began and became fecal. There was no passage of stool or gas from the bowels. On the 10th fecal vomiting continued; temperature was 37.6° C.; pulse small, thready, and very rapid. The abdomen was large and somewhat tympanitic. To the left and on a level with the umbilicus was a painful region about the size of the palm of the hand; pain increased by pressure and percussion, and *something* other than muscular contraction was felt in this region. Internal strangulation was diagnosed and laparotomy performed on the evening of the 10th, about thirty-four hours after the attack began. The abdomen was opened below the navel and a quantity of turbid fluid escaped. The intestines were distended and congested, while other parts of the same intestine were collapsed and pale. Introducing the finger, all seemed free downward and to the right; but to the left a tense, hard body was felt, about 15 centimetres in diameter. Pulling on the distended intestine it was found to run down toward the right hypochondrium, and 80 centimetres were reeled off before resistance was felt. Exposing the part to sight, the intestine seemed to enter an opening like a hernial ring. Gentle traction on the intestine drew out about a metre, when the sense of resistance suddenly ceased, the ring disappeared, and the mass of intestines assumed their normal relations. The circulation seemed restored except that certain parts remained dark. The abdomen was closed, and the patient recovered after having a pneumonia.

Case 7. *Operation; recovery.*—Major W. R. Brown, Indian Medical Service, operated December 21, 1892, on a coolie, aged fifty years, who had been taken with pain in the belly on December 16, soon after eating eight or nine plantains. The bowels moved slightly that day, but not at all during the next five days, in spite of purgatives. The pain continued, and the abdomen increased in size and became tym-

panitic; pain more on the right side. (Nothing was said about vomiting.) Pulse 76, but feeble. Laparotomy through the left rectus below the navel, afterward extended upward. The small intestines were distended and their bloodvessels much congested. No obstruction could be found, so the whole of the small intestine was taken from the abdomen and surrounded with warm cloths. The cæcum was then seen to lie to the *left* of the middle line, and on examining the mesentery it was found to be twisted on itself from *left* to *right*, and was much congested. The coils of small intestine were taken up in the four hands (operator's and assistant's) and rotated in the opposite direction. The cæcum returned to its normal position on the right, and immediately the noise of gas and fluid passing through the bowel was heard, and the bowels moved soon after. Wound closed with drainage tube left in. The patient made a good recovery and was discharged January 23, 1893, and was shown to a medical society February 24, 1893.

In the discussion Captain Smyth referred to the difficulty of recognizing the condition after the abdomen had been opened, and mentioned a case in which the abdomen had been closed without recognizing the trouble, the true condition being brought out at a necropsy. He had seen several cases on the post-mortem table. He stated that the actual seat of obstruction is to be found in the ileum, about six inches from the cæcum, where the gut is so compressed that the mucous membrane is sometimes divided, as in a case he had seen.

Case 8. *Operation; death.*—Monod operated, April 2, 1893, on a girl, aged fifteen years, who was taken six days before with symptoms of intestinal obstruction. First, obstinate constipation (constipation was habitual), resisting the effects of purgatives; then distention of the abdomen, tympanites being greater in the centre than the periphery, as if the small intestine was distended, while the large intestine was not. There was no vomiting; the pulse was a little rapid, but good; temperature, 38° C. The patient complained most of severe pains in the region of the kidneys. On opening the abdomen the intestines presented as an enormous rounded mass, stretched almost to bursting, of a black-greenish color, resembling a cyst. Fluid was found in the peritoneal cavity. The enormously distended intestines were punctured and relieved of gas. The small intestines were found twisted on the mesentery from *left* to *right*, involving nearly all the small intestine. The intestine was untwisted, but retained its black-greenish color (gangrenous), and death occurred the next day.

Case 9. *Operation; death.*—Reynier reported in 1898 the case of a female operated on by his assistant some time before for symptoms of intestinal obstruction. A torsion of the mesentery was found, and it was necessary to remove the entire mass of intestines from the abdomen before they could be untwisted. The patient died.

Case 10. *Operation; death.*—Reynier's second case was a woman, aged fifty years, operated on by him in 1896, seven days after the attack began, with distention, tympanites, and vomiting. He thought at first it was a case of occlusion of the large intestine by a neoplasm. On opening the abdomen the small intestines were found distended, and, searching for the cause of obstruction, a band was found in the right iliac fossa, under which the entire mass of intestines was engaged. He at first thought it was a retroperitoneal hernia, but on drawing on

the band he recognized a twist of the mesentery from *right* to *left*. It was necessary to deliver the intestines from the abdomen in order to untwist them. The veins of the intestines were gorged with black blood, and the intestines were in a gangrenous condition. Death was the result.

Case 11. *Operation; death.*—Kirmisson operated, March 14, 1898, on a boy, aged seven and a half years, who was taken on March 2 with constipation, pain, and vomiting. He got better, and was taken again, March 10, with the same symptoms, and next day there was fecal vomiting. There was no swelling or tympanites of the abdomen, but on the fourteenth day he was much worse, with weak, rapid pulse. The abdomen was opened, the intestines found contracted, the mesenteric veins distended, and a twist of the mesentery was taken for the ligament of Treitz, the true condition not being recognized, and the abdomen was closed. Death resulted.

The necropsy showed a complete torsion of the mesentery from *left* to *right*—about 360 degrees—easily untwisted by turning it in the opposite direction.

Case 12. *Operation; recovery.*—F. J. Shepherd operated, May 9, 1898, on a man, aged twenty-seven years, who had been taken suddenly ill two days before with severe pain just below the navel, and vomiting, which continued. Purgatives had no effect. On admission, pulse 140, temperature 97½° F.; abdomen somewhat distended and tender. Scar of appendectomy done two years before, with a small hernial protrusion, was seen. Laparotomy gave exit to a quantity of reddish serum, and dark-colored coils of intestine presented. Two bands were divided —evidently from the old appendicitis—and the *whole* mesentery was found twisted from *left* to *right*. It was untwisted, the wound closed, with drainage, and the patient recovered.

Case 13. *Operation; death.*—Delbet reported, June 15, 1898, two cases of torsion of the mesentery. Case 1 was a woman, operated on nine days after the first symptoms of intestinal obstruction. She was very weak, with a greatly distended abdomen, which suggested volvulus of the sigmoid flexure; but this was found collapsed, likewise the cæcum. The last coil of small intestine was empty, and on tracing it upward it suddenly bent in and disappeared behind a tense peritoneal fold with a prominent border, upon which the intestine curved from right to left and from above downward. On following it with the finger the impression was given of entering a cavity, which suggested a retroperitoneal hernia. On lifting up the mass of distended intestines a coil of distended intestine was seen by the side of the last coil of collapsed intestine, both engaged behind the sharp border of the peritoneal fold—a circumstance which strongly suggested retroperitoneal hernia. There was apparently a sharp peritoneal fold bounding an opening in which were engaged two coils of intestine—the one distended, the other empty. Traction on the superior, distended, end, in order to reduce the hernia, permitted a slight lengthening, but failed to change the appearance. Traction on the lower, empty coil had no effect. The finger introduced behind the band showed that it was not a ring, and the strangulation seemed due rather to a bend than a constriction. It was impossible to understand the cause which prevented reduction. The coil seemed fixed in the depths. Not understanding the condition, and the state of the patient not permitting further manipulation, an

anastomosis was made between the collapsed and distended coils. The patient died some hours later. The necropsy showed that the anastomosis had been made between two extreme coils of the small intestine —the first coil of the jejunum and the last coil of the ileum. It was finally ascertained to be a torsion of the entire small intestine (mesentery) a little more than a fourth of the way around, as the hands of a watch move. Matters were easily corrected by torsion in the opposite direction.

CASE 14. *Operation; death from pneumonia.*—Delbet's second case was a man, aged sixty-nine years, who was taken suddenly ill, January 30, with violent abdominal pain, especially in the right side; then vomiting and tympanites of the abdomen. Temperature, 37.4° C.; pulse, 100. Laparotomy was done in the evening, about ten hours after the attack began, making the incision below the navel. A quantity of fluid escaped, having the color of that which is seen in strangulated hernia. The small intestine was distended and dark red in color. After enlarging the incision and allowing part of the intestine to escape, the last coil of the ileum was seen collapsed, twisted, and fixed under a peritoneal fold, together with another small coil, red and strongly distended. The ileum, stretched between the cæcum and the peritoneal fold, was immovable, and flat against the posterior wall of the abdomen. The other coil was movable in the middle, one end engaged with the ileum behind the peritoneal fold, and could be easily moved, while its other end, which passed beneath another fold of peritoneum, was fixed. Between the two ends of this distended intestine the mesentery appeared visibly twisted. It was evidently a torsion of the entire mesentery from *right* to *left*. Evisceration was done at once, and the enormous mass of distended intestines was wrapped in hot cloths and lifted up to stretch the mesentery, which was then untwisted by a motion from above downward and from left to right, making a turn and a quarter before the intestines assumed their normal position. The wound was closed, and the patient's condition was good—pulse 90 and temperature 36.8° C.; but bronchopneumonia set in two days later, affected both lungs, and death occurred eleven days after the operation from pneumonia.

CASE 15. *Operation; death.*—John Homans reports in the *Boston Medical and Surgical Journal*, September 29, 1898, page 315, a case of complete torsion of the whole of the small intestine. He said it was the first case he had ever seen, and had heard of only one case since.

A female, aged seven years, was taken, March 24, with pain in the stomach, bowels did not act, pain continued next day, and she vomited. On the 26th she vomited again and kept her bed. There was distention, tympanites, and tenderness at the epigastrium. A band could be felt in the left inguinal region, irregular in shape, and a hard mass was felt with the finger in the rectum. Diagnosis: intestinal obstruction, probably intussusception; and laparotomy in the linea alba, March 29th. Dark-colored fluid escaped on opening the peritoneum, and the small intestine, of a dark purple color and distended, protruded. The entire small intestine was found twisted from *right* to *left* on its mesenteric root. A diverticulum (Meckel's) was found attached. The mesentery was untwisted and the intestines aspirated, removing some gas and liquid fecal matter. They were returned with difficulty and the wound closed, with drainage. Vomiting continued after the operation,

and death occurred at the end of twenty-four hours. Necropsy showed acute peritonitis and patches of gangrene on the intestine.

Case 16. *Operation; death.*—In March, 1899, Delore operated on a man, aged fifty-eight years, who had been taken, four days before, with gradual symptoms of intestinal obstruction, constipation, and tenderness of the abdomen, but he continued at work; then vomiting, becoming fecal, set in, and he was sent to the Hotel Dieu. On the day of the operation the pulse was 120 and temperature 38.6° C. On opening the abdomen turbid fluid escaped. The small intestine was much congested and distended. There was peritonitis, the intestines were fixed, and it was impossible to trace the ileum to the cæcum. It did not seem to be retrosigmoid or retrocæcal hernia. Some bands were found and divided, but they did not relieve, and the wound was closed without finding the cause of the obstruction. The patient died the next day.

The necropsy showed almost the entire ileum twisted twice around its mesentery, as the hands of a watch, from right to left, and the parts were in a condition of gangrene.

Case 17. *Operation; death.*—Major Debrie, of the French army, operated, January 12, 1900, on a soldier who was taken on the 10th with general colicky pains in the abdomen, great weakness, and constant attempts to vomit. No stool for forty-eight hours. Temperature had been 38 2° C.; pulse rapid and feeble. On the day of the operation, temperature, 37.4° C.; pulse, 106; vomiting bilious, but not fecal. Abdomen very much distended and tympanitic. Thinking it might be appendicitis, chloroform was given and the abdomen was opened in the right iliac fossa. A red, turbid liquid escaped, and the intestines were so distended as to be kept in with great difficulty. The appendix was normal, and the patient's condition required arrest of the operation. The wound was partly closed, leaving in a gauze drain. Next day (13th), pulse, 120; temperature, 37.6° C.; no passage from bowels of stool or gas; patient more quiet. On the 14th patient passed some gas; nausea, but no vomiting. Death on the 15th.

Necropsy. The mesentery was found twisted on its axis from *left* to *right*, compressing the ileum two inches from the cæcum at one point, and completely cutting off its communication with the cæcum, and again in the upper part of the ileum, about three-quarters of the ileum being cut off from the rest of the intestine. The intestine above was distended; that included in the mesenteric torsion was dark colored and gangrenous.

Case 18. *Operation; death.*—Morestin operated, March 22, 1900, on a man, aged forty-four years, who had been taken suddenly ill the day before with severe pain in the abdomen, vomiting, and obstinate constipation. At the time of the operation the temperature was normal, pulse 110, and the abdomen distended and tympanitic, especially in the subumbilical region. The intestines were much distended, and, as nothing definite could be found, evisceration was done, when a twist of the entire mesentery from *left* to *right* was seen. It was untwisted by rotating it from right to left, relieving the obstruction, as shown by the cæcum filling with gas. The wound was closed, but death occurred six hours later.

Case 19. *Operation; resection; death.*—Küster operated, May 14, 1900, on a man, aged fifty years, and found rotation of almost the

entire small intestine around the root of the mesentery. It was untwisted and a segment of gangrenous intestine was resected. Death resulted.

CASE 20. *Operation; recovery.*—Major C. L. Williams, of the Indian Medical Service, operated, in February, 1901, on a male coolie, aged about thirty years, who had been sick just twenty-one hours with abdominal pain coming on suddenly in the night. A boggy mass was felt in the rectovesical space by means of the finger in the rectum. The mesentery had made one-half turn (180 degrees) from *left* to *right*, and was fairly easily untwisted. Recovery followed.

CASE 21.—See page 802.

II. (*A*) VOLVULUS IN PART.

CASE 1. *Operation; recovery; return of symptoms; second operation; recovery.*—A man, aged thirty-one years, was operated on at Basle, May 6, 1887, for symptoms of acute intestinal obstruction which came on two days before. On admission, patient was collapsed, cyanotic, pupils dilated, pulse small, abdomen slightly distended, and between the ensiform cartilage and navel a tender *swelling* could be felt.

Laparotomy over this swelling showed a volvulus of the small intestine, one-half turn (180 degrees) of the mesentery. It was untwisted, and two abrasions were seen at the point of torsion.

The patient recovered, but returned on account of constipation, pain in the abdomen, and vomiting, and a second laparotomy was done in the scar of the old one. The great omentum was adherent to the wound of the abdominal wall, and a foot of the mesentery was found attached by a band to the abdominal wall, producing some kinking. The adhesions were dissected loose, the abdomen closed, and the patient recovered.

Sublimate solution, 1 : 5000, was used in the first operation to disinfect the peritoneal cavity.

CASE 2. *Operation; death.*—J. C. Warren operated, August 8, 1887, on a man, aged fifty-two years, who had suffered at times from colic for three or four years. About three weeks before operation he was taken with pain in the epigastrium and back; bowels at first regular, then loose; *no vomiting at any time.* August 8th he became worse, with rapid pulse and great pain about the navel. There was general distention, but a deep-seated, resistant *tumor* as large as an infant's head could be felt near the navel. Median incision over this tumor showed it to be a twisted coil of small intestine, about nine or ten inches long, about the beginning of the ileum. Considerable bloody fluid escaped from the abdomen. The volvulus was untwisted with some difficulty and the wound closed. Death next day.

Necropsy. Incipient peritonitis; mesentery greatly thickened, the veins thrombosed, but bowel in good condition.

CASE 3. *Appendix involved in the torsion; operation; recovery.*—J. Nicolaysen, of Christiania, operated, September 30, 1889, on a man, aged twenty-seven years, who was taken sick on the 25th (five days before), with severe pain in the lower part of the abdomen. The pain left after a short time and came on again on the 29th, with great severity, below and to the left of the umbilicus. There was vomiting, and the abdomen was tensely contracted and tender, especially in the

right iliac region, in which a *tumor-like* resistance was felt. Pulse, 50 to 60; respiration, 30. On opening the abdomen below the navel bloody fluid escaped, and a distended, discolored coil of small intestine appeared, twisted from *left* to *right* about 180 degrees, with the vermiform appendix drawn with it, and forming a tense cord about the twisted point. By turning the coil in the opposite direction the strangulation was relieved, and the appendix returned to its normal position. The appendix was removed and the abdomen closed. Recovery followed.

Within a year following this patient had two attacks of pain in the bowels, vomiting, and obstruction of the bowels, from which he recovered with the aid of medicinal treatment.

Case 4. *Torsion of the mesentery caused by a tumor of the mesentery.*—Charles K. Briddon operated, October 13, 1892, on a girl, aged fifteen years, sick four days. She was taken suddenly with violent abdominal pain and vomiting, which kept up four days. No bowel movement for seven days. Abdomen tympanitic, moderately distended, and tender. Dulness on the right side. Pulse, 102; temperature, 100° F.

Abdomen opened on the right side. Brownish, discolored serum escaped, and a "large coil of moderately small intestine presented, which was of a dark purplish maroon color, and on separating this from other coils a bright yellow tumor came into view, measuring nine inches in circumference." This was found to be a sessile lipoma growing in the mesentery and encroaching on the surface of the bowel for about three-quarters of an inch. There was a twist of the mesentery which appeared to have been caused by axial rotation of the mass. The tumor was enucleated, and the patient recovered.

Case 5. *Traumatic volvulus; operation; recovery.*—G. R. Turner reported, October 24, 1892, the case of a boy, aged seven years, who fell some twelve feet into the mud, striking against the pole of a boat. Collapse soon followed, with vomiting; then restlessness, pain, and tenderness in the right iliac fossa. The vomited matter became fecal. The abdomen was opened twenty-four hours after the accident. A tangled mass of intestines (ileum) was to the left of the middle line, and when this was unravelled two collapsed parts, a foot and two feet in length and separated from one another by about four feet of intervening intestine, were found. The collapsed gut at either end passed abruptly into the healthy intestine. Mr. Turner regarded it as a case of volvulus caused by injury. Uninterrupted recovery followed.

Case 6. *Traumatic volvulus; death.*—Dr. Hawkins mentioned the case of a woman who died with symptoms of acute intestinal obstruction after a slight blow on the abdomen, and the necropsy showed a figure-of-eight twist of the gut behind the umbilicus, which unravelled itself as soon as exposed.

Case 7. *Traumatic volvulus; death.*—Mr. Staveley related the case of a child, aged five years, on whom a slight blow had been struck on the abdomen, followed by symptoms of acute intestinal obstruction and death within twenty-four hours. Necropsy showed a volvulus situated thirty inches from the pylorus.

Case 8. *Volvulus; operation; recovery.*—(Reported by Morris.) Mr. Gould operated, October 2, 1894, on a woman, aged twenty-five years, taken September 29th, after eating lobster, with vomiting and severe

pain in the abdomen; these symptoms continued. The abdomen was slightly distended and tender. Resonance over the front and slight dulness in the left flank. No passage from the bowels since September 29. Temperature, 96° F.; pulse, 120; fecal vomiting of a reddish-yellow color. Abdomen opened below the navel. A volvulus of the small intestine was found, the coils being congested and purple. It was untwisted, and the patient recovered and was discharged October 23d.

Cases 9 and 10. *Volvulus; operation; recovery.*—R. C. Kirkpatrick operated on two cases: (*a*) Operation, November 19, 1894, on woman, aged thirty years, sick three days with pain and vomiting. For a week previous she had cramps. There was constipation; abdomen was tense, slightly distended, and tender to pressure. Temperature, 100° F.; pulse, 78. A volvulus of three feet of small intestine was found, untwisted, and recovery followed. (*b*) Man, aged nineteen years, operated on April 21, 1894. He was taken sick the same day, with swelling of the abdomen, pain, symptoms of collapse; no vomiting. Operated on in the evening. No peritonitis. A volvulus of eight inches of small intestine was found, with a deep constriction at each end. It was untwisted, and recovery followed.

Case 11. *Volvulus caused by straining; resection; death.*—C. B. Lyman operated, October 31, 1895, on a woman, aged thirty years, who was taken sick the day before after doing some heavy lifting. There was pain in the bowels, constipation, and vomiting. The abdomen was tender, and a mass could be felt below and to the right of the navel. At the time of operation—about thirty hours after the attack came on—the pulse was 130, thready, and irregular; the extremities cold. A median incision was made below the navel, when a mass of intestine, black in color, presented. An attempt to untwist it failed, and twenty-seven inches were resected and the ends united by means of a Murphy button. Death occurred before morning. Necropsy showed that a coil of ileum had been twisted, the lower end of the loop being three inches from the cæcum.

Case 12. *Traumatic volvulus; operation; recovery.*—W. P. Giddings operated, February 5, 1899, on a boy, aged fifteen years, who had a fall three days before, and was seized one hour later with abdominal pain, obstipation, and vomiting. The day of operation the abdomen was distended, tympanitic, and tender; pulse, 108, thready; temperature, 97.5° F. On opening the abdomen about 1000 c.c. of bloody fluid poured out; beginning peritonitis was evident. After removing one-half of the small intestine the twist in the mesentery was found and untwisted. The abdomen was closed without drainage, and recovery followed.

Case 13. *Volvulus; operation; recovery.*—J. T. J. Morrison reports, in 1897, the case of a fat woman, aged fifty-three years, taken three days before the operation with severe pain in the bowels, obstipation, and vomiting, which became stercoraceous. No hernia.

On opening the abdomen a large quantity of offensive bloody fluid escaped, and a greatly distended coil of small intestine appeared. This loop was about sixteen inches long, seemed to be the ileum, and was twisted around its mesenteric axis from *left* to *right*. The bowel was deeply congested and ecchymosed, but it was untwisted and returned, the abdominal cavity mopped out, and the wound closed without drainage. Recovery followed.

Case 14. *Congenital volvulus; perforation of the intestine above the obstruction: sigmoid anus; death.*—L. Tissier and R. Mercier reported, in 1897, the case of a female infant, perfectly developed, born September 28th, and who, two days later, became restless, refused to nurse, and began to vomit. The abdomen became distended. Temperature, 36.2° C. Patulous anus; but it was thought that the sigmoid was undeveloped, and operation for artificial anus in the left iliac region was made October 2d. On opening the abdomen a mass of small intestines with a large mesenteric pedicle came out. They were quite red and distended with gas, but contained no meconium. The patient died October 5th, the vomiting having persisted.

Necropsy. General peritonitis, with intestinal contents in the peritoneal cavity. The entire large intestine was empty and about the size (less) of an adult ureter; and 25 cm. from the cæcum there was a sudden torsion of the ileum, the part below ascending in front, the portion above returning below and behind, the two portions making between them an angle of 180 degrees from *right* to *left.* Higher up the intestine was distended, and had given way by a gangrenous slough about the size of a half-franc piece; 40 cm. above was a second torsion, probably due to traction on the distended part.

From December, 1895, to December, 1898, H. Littlewood operated on 7 cases of volvulus—4 of the large intestine and 3 of the small intestine. There were three recoveries—2 of the large and 1 of the small intestine. None of the cases involved the entire mesentery. Only those of the small intestine are given here.

Case 15. *Volvulus; operation; recovery.* (*a*)—Operated on June 9, 1897, on a woman, aged thirty-two years, taken sick June 3d with pain in the abdomen; later with obstinate constipation, vomiting, and abdominal distention. Pulse 150 and full. Ether was given and the abdomen opened in the middle below the navel. Three or four ounces of foul-smelling red liquid escaped. Some coils of small intestine were dark purple in color, distended and adherent to other coils. Fourteen inches of small intestine were found twisted from *right* to *left* on its mesenteric axis, making rather more than one complete turn. It was untwisted, and, though deeply grooved, was left and placed next the incision, which was closed, with drainage. The patient had thrombosis of the right femoral vein, and three days after the operation (June 12th) a fecal fistula formed in the wound, and on the 24th a foot of decomposed small intestine, in the form of a slough, was removed through this opening. She recovered except for the artificial anus, which was closed by a laparotomy and paring and uniting the edges, August 11th. Complete recovery.

Case 16. *Volvulus; operation; death.* (*b*)—Operated May 5, 1898, on a man, aged fifty-three years, sick since April 29th with abdominal pain, vomiting, and abdominal distention, more marked on the left side. Temperature not above normal, but pulse 130. No tumor could be felt. On opening the abdomen blood-stained fluid escaped; purplish-colored, distended intestines were pulled out, and a volvulus involving several feet of small gut was found, the twist being from *left* to *right* on its mesenteric axis, a little more than one complete turn. There was one ulcer in the mesentery at the twisted point. It was

untwisted, but as it remained distended it was incised and a Paul tube was inserted. Abdomen closed, with the intestine fixed in the edges of the wound. The obstruction seemed relieved, but the patient died five days later. No necropsy.

CASE 17. *Volvulus; operation; death.* (*c*)—Operated March 16, 1898, on a man, aged twenty years, taken suddenly ill on the 13th, three days before, in the night, with acute pain about the umbilicus, which continued with vomiting, offensive in character; bowels not opened since the 11th. Abdomen slightly distended, rigid; no tumor. A *doughy sensation* in the pelvis on rectal examination. Under ether the abdomen was opened in the middle line below the navel; some peritonitis; intestines collapsed in the pelvis; distended above. A volvulus of two or three feet was found, the small intestine being twisted from *left* to *right* on its mesenteric axis one turn. It was untwisted and the intestine torn in doing so, but the rent was closed. Patient died on the 18th.

Necropsy showed the small intestine enormously distended over its upper half. The lower four feet formed a partially untwisted volvulus and presented dark, semigangrenous patches.

CASE 18. *Volvulus; operation; recovery.*—Dr. John Rogers (reported by Dr. Elliot, Jr.) operated, July 12, 1897, on a man, aged thirty years; sailor; sick three days with severe abdominal pain, vomiting, and great prostration. Temperature slightly elevated; pulse 120 and feeble. Abdomen swollen and tympanitic, especially in the left iliac fossa. Incision in the median line opposite or through the navel gave exit to bloody serum; small intestine congested. Volvulus found in the lower part of the ileum, which was easily corrected. Vitality of the gut unimpaired. Wound closed without drainage, and recovery followed. Bloody stools followed during the next forty-eight hours especially and somewhat for two weeks.

CASE 19. *Volvulus; operation; death.*—Dr. A. B. Johnson, in 1898, saw a case of volvulus in a child, aged six years, male, sick three days with pain, abdominal distention, vomiting, and rapid pulse. The abdomen, opened in the middle, revealed a volvulus involving about one foot of the intestine about six feet from the cæcum. The part included in the twist was gangrenous, and was resected and an anastomosis made. Death next day. It was found that gangrene extended some distance beyond the section.

CASE 20. *Chronic volvulus; resection; recovery.*—Hadra reported, in 1899, the case of a woman, aged twenty-six years, who had suffered very much for four or five years with the left side of the abdomen, painful at all times, but worse on stooping or bending; a feeling of nausea frequently, bowels more or less regular, tenderness on pressure over the left rectus muscle, and a feeling of resistance opposite the umbilicus, and a *slight swelling* was felt.

Laparotomy over this point disclosed a loop of small intestine double the calibre of the parts above and below, with much thickened walls. At either end was a distinct line of demarcation or circular impression. This coil was quite congested. It was evidently a volvulus, and was resected and a Murphy button put in. The button passed by the twelfth day, the patient recovered, and was free from all her trouble.

CASE 21. *Volvulus; operation; death.*—Dr. Brown saw, in 1899, a colored woman, aged sixty years, who had suffered seven days from

acute intestinal obstruction. On admission the abdomen was enormously distended, and there was fecal vomiting. Suspicion that obstruction was caused by uterine fibroids led to opening the colon in the right lumbar region, without relief; so another opening in front, above the navel, disclosed bloody serum, flakes of lymph, and a volvulus of the small intestine. It was untwisted, and was followed by a gush of fecal matter from the colostomy wound. Death in eighteen hours.

Cases 22 and 23. *Operation on both; both fatal.*—Elosu reports two cases of torsion of part of the mesentery occurring in the service of Lannelongue in March and August, 1900. In one the mesentery had made three revolutions on its axis. Both were operated on, 90 cm. of intestine being resected in one. Death in both cases.

(*B*) Volvulus in Part, Associated Hernia.

Case 24. *Femoral hernia, with volvulus in the abdomen; operation; death.*—Dupuytren operated, in 1819, on a woman, aged seventy-four years, with a left femoral hernia larger than two fists, which had been strangulated twelve days. Taxis had failed. After opening the sac he was still unable to reduce the intestine. Symptoms persisted for two days; the intestine became gangrenous and was incised. There was no relief, and the patient died.

Necropsy revealed adhesions between the coils forming the hernia, and a figure-of-eight crossing in the bowel just before it passed under the femoral arch, the descending passing beneath the ascending portion.

Cases 25 and 26. *Inguinal hernia, with volvulus in the sac; death.*—Zuckerkandl reported, in 1887, two cases of scrotal hernia—one right, the other left—in men, aged, respectively, fifty and sixty-four years, complicated by torsion of the mesentery in the hernial sac. One was operated on, and both died.

Case 27. *Femoral hernia, with volvulus in the abdomen; death.*—L'Honneur reported, in 1856, a case of femoral hernia in a woman. The hernia was reduced, but the woman died in half an hour.

The necropsy revealed a loop of intestine three or four feet long, commencing three feet from the duodenum, twisted upon itself.

Case 28. *Inguinal hernia, with volvulus in the sac; operation; death.*—Dr. Cabot, in 1857–58, reported the case of an elderly man who had a reducible inguinal hernia, for which he wore a truss. It came down during the night, and he was unable to reduce it, and there was pain in the abdomen. Nine or ten hours later he was almost pulseless, and the tumor was about the size of a fœtal head, tense, œdematous, blue, and cold. Operation revealed a large amount of intestine twisted entirely round upon itself and in a state of complete strangulation. Death occurred before next morning.

Case 29. *Femoral hernia, with volvulus in the abdomen; death.*—Laugier operated on a case, reported in 1860, of a woman, aged forty-nine years, who had suffered six days from a strangulated femoral hernia, and found gangrenous bowel, which was opened; but the patient was not relieved, and died eight days after the operation.

Necropsy showed general peritonitis and a volvulus of the lower part of the ileum from *left* to *right* for one complete turn.

CASE 30. *Double inguinal hernia, with volvulus; operation; death.*—J. K. Fowler reported, in 1883, a case operated on by Hulke. A man, aged forty years, who had worn a truss for years on account of a double inguinal hernia, was taken with symptoms of intestinal obstruction. A volvulus of the small intestine was found. Death occurred three days later. The necropsy showed about eighteen inches of ileum near the cæcum, congested and diseased. The whole mesentery was very long—from seven to eight and a half inches from the spine to its intestinal attachment.

CASE 31. *Inguinal hernia, with volvulus in the sac; operation; death.*—C. J. Symonds reported, in 1889, the case of a man, aged seventy-two years, who had had a right inguinal hernia fifty years. It became painful one day, he vomited the next, and herniotomy showed a good deal of omentum in the sac, with a volvulus of the small intestine. This was reduced, but the patient died unrelieved.

Necropsy. No general peritonitis, but thirty-nine inches from the cæcum was a coil of ileum nine and a half inches long, in parts gangrenous, which had evidently formed the volvulus.

CASE 32. *Retroperitoneal hernia, with volvulus; death.*—J. Jackson Clarke reported, in 1893, a case of duodenal (retroperitoneal) hernia in a man who was taken suddenly ill with pain which caused him to fall in the street. At the necropsy Mr. Page found almost the entire small intestine in the hernia. About a foot of the upper part of the ileum was deeply congested—probably the result of having been twisted in the sac. The rest of the small intestine was normal in appearance.

CASE 33. *Double inguinal hernia, with volvulus in the sac; operation; recovery.*—J. T. J. Morrison operated, October 1, 1894, on a man, aged thirty-eight years, laborer, who had had a double inguinal hernia for several years, for which he wore a truss. During a fit of coughing the left side increased very much in size, with agonizing pain bordering on collapse, but no vomiting. Operation five hours later. Blood-stained fluid escaped on opening the sac, and about a yard of small intestine, which was only slightly congested; but another coil, about twelve inches long and very dark in color, was seen deep in the sac. This loop was twisted around its mesenteric axis, and was evidently the cause of the acute symptoms and blood-stained fluid. The intestine was untwisted, reduced, and the radical operation for cure performed. Recovery followed.

CASE 34. *Retroperitoneal hernia, with volvulus; operation; recovery.*—Neumann reported, in 1897, the case of a woman, aged fifty-five years, who was taken, six days before operation, with sudden cramps in the abdomen, vomiting which became stercoraceous, and obstinate constipation. Abdomen moderately distended and tender. Operation disclosed a right duodenal hernia, the sac containing the bowel lying to the right of the spinal column, and forming a tumor larger than a child's head. Part of the intestine was withdrawn by traction on the lower part (ileum), when it suddenly ceased, and examination showed a loop of bowel twisted into a pedicle. It was untwisted with difficulty in the sac and withdrawn. It was about half a metre long, blackish-blue in color, surface dull in places, and the mesentery was œdematous and contained infarcts. Recovery followed.

CASE 35. *Umbilical hernia, with volvulus in the abdomen; death.*—R. L. Knaggs operated, May 17, 1897, on a woman, aged sixty-two

years, with a large strangulated umbilical hernia. She was taken the day before with intense pain in the hernia and vomiting. Operation six and a half hours after the attack began. Pulse 54 and of good volume. Blood-stained fluid and several feet of small intestine, distended and black with blood, were found in the sac. There was no constriction at the hernial ring. The opening was enlarged and the intestines withdrawn until healthy bowel was reached; then a volvulus involving between four and six feet of small intestine was found and released by a half turn and the intestine returned. The patient had some relief, and passed feculent matter and sanious fluid, but death occurred after forty hours. No necropsy.

Case 36. *Scrotal hernia, with volvulus in the abdomen; operation; death.*—R. L. Knaggs operated, October 4, 1898, on a man, aged fifty-six years, who had long suffered from a left irreducible inguinal hernia. He was taken thirteen hours before with pain in the umbilical region, followed by vomiting, swelling of the hernia, and seven or eight hours later the passage of a quantity of bloody fluid and clots. Pulse 84.

On opening the sac, dark fluid and about three feet of small intestine were found—a part almost normal and the other part congested and covered with bloody fluid. The trouble was not at the abdominal rings, and the finger introduced detected something like a band inside. The intestine was drawn down until it became healthy, when a constricted point was found. As the patient's condition was bad, the intestine was reduced, in the hope that the volvulus would untwist, and the wound was closed. Death occurred twenty-seven hours later.

The necropsy showed that the lowest four feet had made a single half turn from right to left, "so that at the neck of the volvulus the termination of the ileum lay over and directly across the ileum at a point some feet above the valve." The greater part of the loop had been in the hernial sac. Cause of death suggested was shock and fecal intoxication.

Case 37. *Femoral hernia, with volvulus; resection of gangrenous part; recovery.*—Dreesman operated, May 7, 1898, on a woman, aged thirty-seven years, with a right femoral hernia. She was taken the day before with pain, swelling of the hernia, which became as large as two fists and tender, and vomiting. Pulse 160. On opening the sac dark-colored fluid escaped, the intestine was gangrenous, and the gangrenous portion extended into the abdomen and could not be drawn out. The abdomen was opened by extending the hernial incision, when more dark fluid escaped, and a volvulus of the lower part of the ileum, from *right* to *left*, one half turn, was found. About 7 feet (2.15 metres) of gangrenous intestine were resected and the proximal end inserted laterally into the colon. Recovery followed.

Case 38. *Inguinal hernia, with volvulus in the sac; operation; recovery.*—J. C. Da Costa reported, in 1899, the case of a man, aged forty-nine years, with an old, very large inguinal hernia, which nothing would retain in place. Three days before operation there had been pain in the hernia and in the abdomen, tenderness and nausea, but no vomiting. The sac contained the cæcum, appendix, most of the ascending colon, and a considerable portion of the ileum and omentum. A portion of the ileum was found twisted, adherent to surrounding structures, deeply congested, and strangulated. The omentum was removed, the intestines reduced, and the patient recovered.

CASE 39.—See page 803.

CASE 40. *Femoral hernia, with volvulus in the abdomen; death.*—This patient, seen by me, was a white woman, aged sixty-two years, who had had a left femoral hernia many years. It came down on the night of April 24, 1902, and she was unable to reduce it. Next day she was in pain, and began to vomit. When I first saw her, on the 26th, the abdomen was soft, not swollen, but was tender, as was the hernia. Pulse 120, and vomiting was stercoraceous. Patient refused operation, and died about forty-eight hours after the first symptoms appeared. Necropsy showed slight peritonitis, but considerable effusion of dirty yellow serous fluid. The hernial sac contained about one inch of gangrenous ileum about twelve inches from the cæcum, tightly constricted by the femoral ring. Within the abdomen was a distended coil of intestine continuous with the portion in the hernial sac. The coil formed a volvulus about two feet long by turning on its mesentery from right to left a half turn, and was held in place by the hernia. Reduction of the hernia permitted the volvulus to untwist.

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INTESTINAL PERFORATION DURING THE COURSE OF TYPHOID FEVER, AND ITS SURGICAL ASPECTS.

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Frequency and Mortality of Perforation. While the percentage of deaths resulting from typhoid fever, and more particularly the proportion of these deaths due to perforation of the bowel is a well-established fact and quite generally known, we believe that the specific appreciation of the appalling number of these individual cases of perforation is by no means appreciated by the medical profession in general. While we all appreciate that the death rate from typhoid fever is from 7 to 14 per cent., averaging, probably, for the entire United States about 10 per cent., and that of these fully one-third are due to perforation, we think that few could have read without marked surprise the statistics recently collected by Dr. H. M. Taylor in an article on "Typhoid Perforation: Its Frequency, Prognosis, Diagnosis, and Treatment," *New York Medical Journal*, February 1, 1902, vol. lxxv. p. 193. From various statistical sources gathered in 1896 the author has determined the number of cases of typhoid fever in the United States as about 500,000 per annum, and the death rate about 50,000, which is doubtless a very fair average mortality. The frequency of perforation has been so definitely established from so many sources as being about 33⅓ per cent. of the deaths, that this number can hardly be questioned. This would give a death rate of something over 16,660 cases from perforation in typhoid fever in one year in the United States. Of this number it is now definitely known that 5000 to 8000 cases annually can be saved by operative interference. These figures represent, we believe, an adequate appreciation of the usefulness of surgical interference in the United States at the present time, and are certainly striking and instructive.

Owing to the very rapid medical and surgical progress along the lines of diagnosis and treatment in typhoid perforation during the last five years, the usefulness of operation in such cases has become established so far beyond the possibility of any doubt that it is no longer found necessary to urge and justify the procedure in the large majority of the cases. The question of recovery in such cases without operation is a matter of very grave doubt, although it has been absolutely known to occur in a few isolated instances where the damage was well localized near the cæcum, the cases assuming more the characteristics of appendicitis than those of perforation. It is an unwarrantable assumption, however, that unoperated cases recovering from mild or even

marked symptoms of perforation are actual cases of recovery from perforation itself. At a time when medical treatment was practically the only means employed, the possibility of recovery was a very serious question even among the best authorities. In an article by Dr. R. H. Fitz (*Transactions of the Association of American Physicians*, 1891, vol. vi. p. 200) on "Intestinal Perforation in Typhoid Fever: Its Prognosis and Treatment," the author states: "Since perforation of the intestine in typhoid fever may take place without any subjective symptoms, and since suggestive—even so-called characteristic—symptoms may occur without any perforation having taken place, it must be admitted that recovery from such symptoms is no satisfactory evidence of recovery from perforation." Any practitioner who has been intimately associated with typhoid fever for any length of time has seen cases of typhoid suggesting perforation that have gone on to recovery, but too often there has been an unwarranted assumption that perforation actually occurred, and the instance has been mentioned as a remarkable cure. Since the usefulness of operation has been established in these cases it has become a well-known fact that the gravest symptoms of perforation may be present without the actual lesion, and, on the other hand, a rather premature assumption from vague symptoms has been absolutely justified by the discovery of perforation at operation. It is needless to say that these remarks apply to the diagnosis of perforation and not to the diagnosis of general peritonitis following perforation. The same position, however, the lack of signs and symptoms corresponding to the actual pathological condition, has been long since established with reference to general peritonitis that has recently been demonstrated with reference to typhoid perforation. The man who assumes an unassailable position in either one of the above-mentioned conditions in instances which cannot be subjected to actual demonstration, can no longer be considered to hold a tenable and justifiable position. It must be admitted at the present time that it is a far safer and much more justifiable assumption that the mortality in unoperated cases of intestinal perforation in typhoid fever is practically 100 per cent.

It was eighteen years ago that the first operation for perforation was performed. Dr. W. W. Keen, in 1898, in his book on *Surgical Complications and Sequelæ of Typhoid Fever*, published a table of 83 cases collected by Dr. T. S. Westcott, and in the *Journal of the American Medical Association* for January 20, 1900, in an article on "The Surgical Treatment of Perforation of the Bowel in Typhoid Fever," the same author gives a table of 75 additional cases collected by Dr. M. B. Tinker, 158 cases in all, which were considered to include all the cases published to January 1, 1900. Since that time the number of published cases has rapidly increased, but owing to greater familiarity

with the subject and the increased frequency of operation it is believed that the number of published cases is far below the number of operations performed, especially in unsuccessful cases. The majority of the reports have been glaringly incomplete, indicating either a deplorable lack of scientific observation, or failure on the part of the writers to appreciate the increasing necessity for careful and detailed reports in such cases. The grosser and more evident facts with reference to diagnosis have already been well established, but the refinements in diagnosis which are going to make it possible to detect the occurrence of this complication at a much earlier stage and in a much larger proportion of the cases are still lacking. The question of general peritonitis ought not to enter at all into the consideration of perforation. Many of the pathognomonic signs, so-called, of perforation are now known to be merely an indication of general peritonitis. It is only by keeping these two conditions distinctly separated in the general medical mind that the diagnosis of perforation is to be more frequently and more accurately made, and it is only by strict and careful attention from now on to the refinements of diagnosis that we shall be saved the humiliation of operating for perforation and so frequently finding extensive peritoneal infection. Much improvement in operative technique at the present time cannot be expected, as this has already reached as advanced a stage of perfection as our present surgical knowledge will permit. Improvement is to be looked for almost entirely along the line of early and accurate diagnosis, which can only be the result of careful clinical observation, and what is of equal or even greater importance, of accurate pathological study. The pathology of these cases, especially the information afforded by extended post-mortem examinations in unsuccessful cases, has been even more neglected than the clinical study, whereas the whole question of prognosis and of the causes of death depend absolutely upon post-mortem findings. With but relatively few exceptions it has been assumed that the mortality following operation has been due to general peritonitis. It cannot be denied at the present time that this is not for the most part a correct view, but the comparatively few post-mortem examinations recorded certainly indicate that a good many of the unsuccessful cases die from causes entirely independent of the operation, and which at the present time are beyond means of control. It is in the hope of stimulating interest in the more uncertain points of diagnosis, and especially in the pathological knowledge of these cases, as well as affording some definite suggestions for accomplishing these objects, that the present article is presented. Many of the observations contained in this paper have been suggested by cases of typhoid perforation studied at the Lakeside Hospital in Cleveland during the last four years, several of which were reported by the writer from the surgical clinic of the hos-

pital in The American Journal of the Medical Sciences, January, 1902, vol. cxxiii. p. 38, "Laparotomy for Perforation in Typhoid Fever."

It may seem at first that it requires considerable temerity to speak of the diagnosis of typhoid perforation from a purely surgical standpoint. The view of the medical profession, however, has changed so radically with reference to the treatment of perforation, that it may almost be said to come under the head of a surgical rather than a medical complication, in the same manner in which appendicitis is now brought to the observation of the surgeon, not solely at a time when operation is immediately demanded, but for the sake of diagnosis in doubtful or somewhat obscure conditions. Surgical aid in the diagnosis of appendicitis has become of the utmost value, and we feel equally certain that much the same consideration will prevail with reference to typhoid perforation. It is largely on this account that the surgical interest in typhoid fever in general has recently become so manifest. The physical conditions of the abdomen are often so altered during the course of typhoid fever that the surgeon who is unfamiliar with the typhoidal abdomen is utterly incapable of giving a well-considered opinion in cases of suspected perforation. It was in view of this fact that Dr. Osler, a few years ago, so strongly urged the desirability of surgical observation of the typhoid cases at the Johns Hopkins Hospital, and it is largely on account of the lack of opportunity for such observation among surgeons in general that so little has been done on the subject outside of large hospitals. The desirability of surgical familiarity with the abdominal conditions in all stages of typhoid fever cannot be too strongly urged, and its importance cannot be over-estimated.

Etiological Considerations. In considering the subject of intestinal perforation in typhoid fever, there are a number of points in the etiology of the condition which have already been determined with all the accuracy that is desirable, and which can be dispensed with in a few words. The *time at which the perforation occurs*, so far as diagnosis is concerned, is of no consequence. It most frequently occurs during the third week, but in one of the Lakeside series there were very marked suggestions of perforation in one case on the fifth day of the disease, although no perforation was found, and in another case general peritonitis had followed a perforation occurring on the sixth day, as nearly as could be made out from the history. It may occur late in a prolonged convalescence, or in a relapse, so that from a standpoint of diagnosis the stage at which the patient has arrived in the illness must be entirely overlooked. The time of perforation is of much consequence, however, with reference to the general condition of the patient and to the way in which operation is borne, as will be

mentioned later. The *severity of the fever* can be overlooked entirely in diagnosis, except for the fact that diagnosis is more difficult in severely sick cases, where one scarcely ever finds the indications so marked. It is the opinion of Dr. Osler that it occurs more frequently in severe cases; but medical opinion in general is quite divided, and from the study of the reported cases one is certainly justified in a conservative opinion. It certainly appears to occur about as frequently in mild as in severe cases, and in any event it occurs so frequently in both classes that the mildness or severity of the disease can be entirely laid aside with reference to diagnosis. The matter of *constipation and diarrhœa* is of little consequence in diagnosis, the cases being so equally divided that these conditions can also be overlooked. The question of *age and sex* is of slightly more importance, but this also can be overlooked almost entirely. It occurs much more frequently in young adults, but three or four cases have been reported in children under fifteen years. It also occurs much more frequently in males than in females. Neither of these conditions can influence the diagnosis to any appreciable degree, however, except that one might be justified in delaying a little longer in cases of young children. It is of somewhat curious interest that only two instances of operation for perforation in a negro have been reported, and that in only one of these was perforation actually found. The question of *intestinal hemorrhage* is of somewhat more importance, but mainly from the fact that its occurrence at the time is very apt to mask or simulate perforation and render diagnosis much more difficult. As an etiological feature, however, antecedent to perforation, we believe it can be entirely overlooked. The occurrence of hemorrhage is purely fortuitous, and depends solely upon the chance of the ulcerating surface encroaching upon a vessel of considerable size. It cannot be assumed that the ulcer is approaching the peritoneal surface more rapidly on that account, or that the process will even eventuate in perforation merely because the hemorrhage has occurred. A comparatively small number of the reported cases of perforation have been preceded by hemorrhage, and it is only a small percentage of the cases of hemorrhage that have eventuated in perforation. In instances where the relation is suggested it is almost invariably a mere assumption that hemorrhage has come from the particular ulceration that has gone on to perforation. So that in considering the diagnosis of perforation we think one can entirely overlook as etiological factors the period of the disease in which the perforation occurs, the severity of the disease, the occurrence of constipation or diarrhœa, the question of age, sex, and color, and the occurrence of hemorrhage from its purely etiological standpoint.

Symptoms and Signs of Perforation. In considering the *symptoms and signs* of perforation we believe it is of the utmost importance

to preserve a sharp distinction between the two. Some of the signs of perforation are doubtless always present, although possibly unobserved or misinterpreted. The amount of dependence one can place on symptoms, however, depends entirely upon the mental condition of the patient and his appreciation of sensations. The patient whose faculties are moderately alert can afford very material aid through his perception of pain and his own conception of being very much worse or very much better. In proportion to the amount of apathy so often present to a greater or less degree, these sensations are much less acute, and the patient's ideas regarding himself are of much less consequence. In deeply apathetic or delirious cases the question of symptoms must almost invariably be largely or entirely set aside. Consequently in the latter class of cases, which are almost always the severely sick cases, one must rely almost entirely upon physical signs and phenomena. As in so many other conditions, in the cases in which one is most desirous of making an early and careful diagnosis, the means at hand for making this diagnosis are much more strictly limited than in less severe cases where one can risk a little larger margin of error. It is thus evident that in most severe cases one is forced to be more radical in his diagnosis and establish the presumption of perforation on somewhat less sufficient grounds. These two distinctions, then, between signs and symptoms on the one hand, and the clear-minded as against the apathetic and delirious patients on the other, at once assume proportions of the very highest importance, and it does not seem to the writer that these considerations can be too strongly urged. These are distinctions to which we feel justified in making frequent reference.

Symptoms. In considering first the symptoms of perforation one finds for consideration pain, sensitiveness, the sensations associated with systemic shock, and the sensations of altered respiration. These have been named in the order of their relative importance in the vast majority of cases in which the sensibility of the patient is sufficiently acute to make them of any use whatsoever.

Abdominal pain is by far the most important symptom, and if present demands the utmost consideration in forming a diagnosis. This is especially true where the patient has been comparatively free from previous abdominal complications and the symptom appears as a sudden, sharp, often agonizing sensation, quite circumscribed, located in the lower part of the abdomen near the median line or toward the right side; and especially if the pain remains severe and circumscribed for an hour or more. Such a picture one can scarcely mistake, and with a very slight suggestion along the line of physical signs one must feel justified in making the diagnosis. The pain, however, may come on gradually, commencing almost anywhere in the abdomen, but more frequently starting near the median line, near or below the umbilicus.

If the pain is general at the start it usually becomes more closely confined to the lower half of the abdomen within a short time. When pain becomes more general after having been moderately well localized at the start, it suggests rather strongly that peritoneal infection is progressing from a point of perforation. The pain, whether sudden or general in its first manifestations, localized or diffuse, may at the same time be either moderate or severe; in general it can be said that the better localized the pain the more keenly it is appreciated, but the distinction is of vastly less consequence than the fact itself that pain is present. So that the occurrence of pain is a feature of the utmost importance when present. The location of the pain, its limits, its severity, the manner of appearance, and persistence are matters of secondary importance, except possibly the last-mentioned feature. In proportion to the degree to which these various features of the pain are accentuated these secondary considerations of pain may be said to be of importance, but the absence of such accentuation must be almost entirely overlooked in arriving at a diagnosis.

Sensitiveness is, of course, very closely allied to pain, and may almost be considered as a less strongly marked manifestation of the same sensation, so that many of the things mentioned with reference to pain are true to a less degree with reference to sensitiveness. All patients with abdominal pain are sensitive, but one is often obliged to rely considerably upon sensitiveness as a symptom in the absence of pain. The limits of sensitiveness are usually more narrow than those of pain, and on this account it is sometimes of aid in assisting the patient to more definitely locate his pain. Localized pain is accompanied by localized sensitiveness, but diffuse pain is not infrequently associated with circumscribed sensitiveness, and this fact is often an aid of considerable importance. Spreading sensitiveness is open to the same interpretation as spreading pain, and is if anything a little more to be relied upon. The occurrence of sensitiveness is more common to the lower half of the abdomen or to the entire right half. Its frequent occurrence in the right lower quadrant, to which attention has been strongly called by several writers, does not appear to exist in many cases. The truth of this statement has been strongly suggested by the Lakeside series and seems to be justified by the large proportion of reported cases. The degree of accentuation increases the usefulness of sensitiveness, also, as a symptom, possibly a trifle more so than in cases of pain; but here again the characterizing features of sensitiveness are of only secondary importance as compared with the presence of sensitiveness itself.

The *sensations associated with systemic shock* vary so greatly in different patients, and are so closely allied to certain signs to be mentioned later, that one is obliged to speak of them in a very general way. These

sensations, general and varying as they are, however, in a responsive and clear-minded patient are worthy of careful consideration when present. Perhaps their meaning is best described by the expression so often used by the patient himself, literally or implied, of an "all-gone feeling," as if the "bottom had dropped out of him;" a feeling vaguely described but strikingly realistic, that some serious catastrophe has occurred. It is doubtless this that sometimes causes in these patients the intensely anxious and apprehensive countenance not infrequently seen, the exact meaning of which they are unable to put into words. It is scarcely possible to speak of these sensations in more detail. Their presence is unmistakable and of considerable importance; their absence, again, may be entirely disregarded in making a diagnosis.

The *sensations of altered respiration* are of little consequence compared with the other symptoms mentioned, or compared with respiration as a sign. The patient is apt to feel short of breath, and finds that his respirations for some reason or other must be largely costal. As a sensation it is present in almost direct proportion to the intensified characteristics of pain already mentioned, and in the absence of pain, at least in the absence of pain and sensitiveness, it does not exist. The symptoms of altered respiration are of so little consequence that they may be entirely disregarded.

Signs. But it is upon the signs suggesting perforation that one is forced to rely largely, and in apathetic and delirious cases one must rest his diagnosis upon these signs almost absolutely. Here, however, it is necessary to draw the distinction even closer between perforation and general peritonitis, and keep in mind that the diagnosis of general peritonitis is not the diagnosis of perforation. And against maintaining this distinction one cannot with propriety set the fact that both these conditions at times are very bizarre and misleading in their manifestations, and that occasionally the postmortem examination reveals a condition of which the manifestations before death gave absolutely no recognizable indication. These signs suggesting perforation include, first, indications gathered from the abdominal examination alone, such as muscular resistance, the presence of gas within or outside of the intestine; and, second, certain general systemic indications, such as vomiting, altered respiration, temperature, pulse, altered blood conditions, and general systemic shock.

Muscular resistance is, we believe, the most important of all these signs. It is a sign of the utmost importance in almost any acute intra-abdominal condition, and its reliability can rarely be questioned with impunity. It indicates very clearly that the abdomen is trying to protect itself against injury from the outside, and is a condition largely independent of the volition of the patient. The presence of pain and sensitiveness is, to be sure, usually associated with muscular resistance

to a greater or less degree, but the same patient, if he is deeply apathetic or delirious, and abdominal protection is still needed, would show muscular resistance. This muscular resistance is not infrequently general, but in cases of perforation in typhoid fever, since the lesion is almost invariably located in the lower half of the abdomen or on the right side, the resistance is accentuated in these localities. Its usefulness is impaired to an inexperienced observer, however, in that many cases of uncomplicated typhoid show a varying amount of muscular resistance which must not be mistaken by one seeing the case for the first time. Here, again, is a very striking example of the necessity for surgical familiarity with the abdominal conditions in uncomplicated typhoid, and also of the great desirability of having typhoid cases under frequent surgical observation. Muscular resistance is probably never absent in perforation. If resistance was present before perforation it is probably always increased, and in such cases an accurate estimation of the degree of increased resistance is of great value.

Distention and tympany from gas within the intestines are signs of no consequence with reference to perforation *per se*. Their absence is of equal inconsequence. As signs of spreading peritoneal infection, however, they are both of well-known and merited consequence and need not be discussed here. They are confirmatory evidences only in so far as one has been willing to run the risk of spreading infection secondary to the perforation. If there was gas in the intestines previous to perforation, as is frequently the case, it would not be increased by the accident; if the abdomen was soft and there was no distention one would not find a sudden accumulation of gas when perforation occurred. So that aside from the fact that distention and tympany may tend to obscure the diagnosis and render it more difficult they can both be set aside entirely with reference to the diagnosis of perforation itself, and are confirmatory only in proportion to the degree of spreading infection.

The presence of *abdominal gas outside the intestine*, however, if its presence can be demonstrated with certainty, is practically a proof of perforation. Such evidence is usually sought through obliteration of the liver dulness. This manifestation, however, is a matter of such uncertainty that it renders the interpretation of the sign of practically no value. The obliteration of liver dulness has been demonstrated again and again to be due to a distended colon or small intestine as well as to free abdominal gas, and in several cases in which diagnosis was considered practicaly absolute on account of this sign, no perforation was found. The absence of altered liver dulness is, of course, a matter of absolutely no consequence in diagnosis, and in cases where the liver dulness is altered to an appreciable extent, it is quite impossible to say whether it has been effected by free abdominal gas or dis-

tended intestine. If the liver dulness is altered one may be justified in being suspicious of the circumstance, but we feel he is unjustified in any further assumption.

Nausea and vomiting occur so infrequently that they are of little aid in the diagnosis, and their absence may be entirely set aside. They are more frequently associated with cases in which there is severe pain, and in these cases are probably open to the same interpretation as nausea and vomiting under any condition of severe abdominal pain. They are also seen, however, as manifestations of severe systemic shock, but in such cases the presence of shock is so manifest that one need not look for the confirmatory evidence of vomiting. They occur in less than 25 per cent. of the cases. Their presence is of slightly confirmatory value only.

Altered respiration is a sign of consequence, and is probably to be interpreted as muscular resistance, namely, a means of protecting the abdomen. The prevailing type of respiration where perforation has occurred is almost invariably distinctly thoracic. This type of respiration is also seen in severe cases of typhoid with distention and rigidity, but the phenomenon is considerably accentuated when perforation occurs. It was a very striking sign in all the Lakeside cases. It is rather more evident, to be sure, in clear-minded patients with considerable pain, assuming somewhat the quality of a symptom; but it is sufficiently recognizable as a sign alone where the mental condition of the patient is to be entirely disregarded. The rate of respiration, also, is nearly always more or less increased, but is of largely secondary consequence. If the patient is in pain, respiration may be unduly increased on this account alone; if he is insensible to pain, the restricted respiratory excursion will necessitate somewhat more rapid breathing. Altered respiration, then, of the costal type warrants much the same assumption as muscular abdominal resistance, and we believe this alteration can be found in practically all cases if sufficiently well observed. As this alteration is largely relative it is probably less reliable than muscular resistance, and as it is open to the same interpretation its practical value, aside from being merely confirmatory, is not great. Its absence, however, as in the case of muscular resistance, must be considered of considerable importance.

Alteration in temperature may be of some positive value, but the absence of such alteration must be set aside entirely in making a diagnosis. An accompanying chill is of rather infrequent occurrence. Two of the Lakeside cases showed no alteration in temperature, and many other reported cases are equally negative in this respect. Many cases will show a rise or fall generally not exceeding 2° F., which, when considered with the usual irregularity of the typhoid chart, must be admitted to be of little value. A very decided drop in temperature,

as is sometimes seen in hemorrhage, is rather less frequently met with in perforation, we believe, than has been generally supposed. As an indication of spreading infection the value of altered temperature has long since been well established, as was mentioned also with reference to distention and tympany; but as an indication of perforation itself the matter of altered temperature may be very largely overlooked.

The *pulse* is an indication of greatest importance. It is, of course, an evidence of systemic shock accompanying perforation, but is a matter of such consequence that it deserves special mention. One can almost invariably expect a rise in pulse that is quite marked, perhaps twenty beats or more, the alteration occurring rather suddenly. This rise in pulse is affected in a measure by the increased respiration, but is almost always too marked to be accounted for entirely on such grounds. The quality of the pulse also is markedly altered, the tension being reduced, and the pulse rendered readily compressible. These strikingly distinctive changes in the rate and quality of the pulse are, of course, less strongly marked in more severely ill cases, in which the pulse is already rapid and the quality poor, but even in such cases, to one familiar with the daily condition of the patient in question, the relative alteration is evident. It may also be of some aid in differentiating between shock and hemorrhage, as alteration in rate and quality is likely to be more gradual in hemorrhage; it is a distinction, however, that is by no means always recognizable, but may serve as a somewhat confirmatory observation. Sudden marked alteration in rate and quality, then, is an indication of great importance.

Definite knowledge regarding *altered blood conditions* occurring in typhoid fever is so meagre that we feel that little reliance can be placed upon it in making a diagnosis of perforation. This may appear at first sight to be a rather striking and radical statement. In the large proportion of cases it is very doubtful if *the white blood count* is affected by the perforation itself. It is true that in many instances a leucocytosis is observed to follow perforation at an interval of anywhere from one to six hours; but, on the other hand, in a very considerable number of cases no such leucocytosis is observed. It has also been observed that moderately sudden and quite extreme leucocytosis occurs in patients in whom perforation was supposed to exist, when operation showed definitely that none had occurred. One of the Lakeside cases showed such a rise from approximately 8000 to 50,000. It has been assumed by some and considered demonstrated by others that following perforation there is a "wave of leucocytosis" extending over a period of a few hours, and that in cases where no leucocytosis is observed the observation has been made at the close of this wave. Some cases show this condition, others do not. Whatever one's belief regarding it may be, it is known to be a certainty that the leucocytic equilibrium in man

is very easily disturbed to a greater or less extent. Some of the causes that at times effect this disturbance are known with a moderate degree of certainty, but the number of causes with which we are somewhat acquainted is probably very small as compared with the number of causes for which we are utterly unable to afford any adequate explanation at the present time. Slight temporary differences in the white blood count are usually beyond explanation, and while it may be assured that such temporary flights occur in perforation it is an assumption that must be based upon far wider and much more accurate observation than has been made thus far. These waves of leucocytosis have been demonstrated to exist in many conditions, and for that matter in supposedly normal individuals, which had they occurred in conjunction with symptoms suggesting perforation might be assumed to be due to that cause. One such set of observations has been made by Cabot, Blake, and Hubbard in an article on "A Study of the Blood and Its Relation to Surgical Diagnosis," *Annals of Surgery*, vol. xxxiv. p. 361. These views are based upon the observation of only ten cases, to be sure, four of which were typhoid fever, but they are as extended and certainly more accurate on the whole than any observations in favor of the leucocytic wave theory in perforation, and serve to put the subject where one is unable to attach to it much diagnostic importance at the present time. What may, however, prove to be of some consequence is a steadily increasing leucocytosis reaching a well-marked maximum, which is attained after a considerably longer period than the height of the so-called wave. The interpretation of this increase, however, is largely an assumption; it may be due to spreading infection which has not yet become sufficiently marked to cause the fall in the number of leucocytes not infrequently seen in cases of extensive peritoneal infection. Be this as it may, it must be admitted to be of relatively small practical importance, for if these cases are to be saved one must not wait for a well-developed leucocytosis from any such cause. There is a great though apparently decreasing tendency to overestimate the value of leucocytosis in surgical abdominal conditions at the present time, and we feel that this is an example. The irregularity noted in the blood examinations in cases of demonstrated typhoid perforation is so great that the subject needs far wider and much more accurate study than has thus far been given. But while from the standpoint of diagnosis the question of leucocytosis must be largely set aside, from the standpoint of careful and complete observation of cases the importance of such examination cannot be overestimated. The subject may have possibilities; before leaving it the absence of such possibilities must be thoroughly demonstrated.

Alteration in the amount of *hæmoglobin* and the number of *red blood corpuscles* in these cases is a matter that has been almost entirely over-

looked, but from a theoretical standpoint it would appear to be of somewhat more consequence than the white count. The most difficult cases for diagnosis are those in which the decision lies between hemorrhage and perforation. If the diagnosis of hemorrhage is incorrectly made, and instead of this perforation has occurred, the desirable opportunity for operation is lost while waiting for the demonstration of hemorrhage through the bowel discharges. It may be possible to make use of the red count and the estimation of hæmoglobin as affected by hemorrhage to aid in the differential diagnosis in these cases. The white count can be of little aid in this differentiation. It is felt that some careful observations along this line will prove valuable.

Systemic shock is probably always present, although not always recognized, and is an indication of the very greatest importance. The condition is usually so evident and its indications so readily recognizable that it is scarcely necessary to consider it in detail other than to insist on its importance. Altered respiration to a slight degree possibly, and especially alterations in pulse, temperature, and blood are indications of general systemic change. The pallid countenance, the drawn facial expression, slight cyanosis of lips and finger-nails, the sudden occurrence of perspiration, and the slight tremor that is sometimes present, together with the altered pulse and temperature, make a very striking picture when well marked. Here, again, however, in proportion as the organism is deeply affected by the disease itself, the margin of vitality susceptible to even the severest degree of shock is narrow, and the system may be so deeply affected that it fails entirely to respond in any appreciable degree to the shock received, and the catastrophy passes unrecognized. It must be kept in mind, however, that this is said solely with reference to the severity of the infection, and is entirely independent of the mental condition of the patient. Shock is distinctly recognized by physical, not mental demonstrations, and if any reactionary power remains in the organism the condition can be recognized in spite of delirium or apathy. This condition of systemic shock was observed in all of the Lakeside cases. In one case with severe infection and moderately well-marked shock no perforation was found, and the cause of the suddenly altered condition was never demonstrated.

In summary, then, the signs and symptoms upon which one is forced at the present time to rely mainly in making a diagnosis of perforation are *pain, sensitiveness, muscular resistance, altered respiration, alteration in rate and quality of the pulse, and evidences of systemic shock.*

Differential Diagnosis. The question of differential diagnosis is a matter upon which there is little to be said with satisfaction, owing largely to our fragmentary and quite indefinite knowledge of the causes of pain during the course of typhoid fever. Pain must be considered a most important symptom, and at times the most important

feature in making the diagnosis of perforation, but at the same time it is the indication which most often leads us astray. A most instructive and commendable paper by Dr. Thomas McCrae, "Abdominal Pain in Typhoid Fever," *New York Medical Journal*, May 4, 1901, vol. lxxiii. p. 749, is perhaps the most valuable article of its kind that has occurred in the more recent literature. His report is based upon the analysis of 500 cases at the Johns Hopkins Hospital, in which it was found that only two-fifths of the patients were free from pain or tenderness; one-fifth showed tenderness only, while two-fifths showed pain sometime during the attack. Of this number there were only 13 cases of perforation, while in 70 cases there was no discoverable cause. It must be admitted that in a large proportion of cases in which the existence of perforation has not been demonstrated at operation, the causes of the indications leading to the diagnosis have not been discovered, and in instances in which the causes have been assigned it was largely an assumption. Among these causes, known or supposed, are diaphragmatic pleurisy, pneumonia, iliac thrombosis, appendicitis, peritonitis from undiscoverable causes, intestinal obstruction, suppurating mesenteric or retroperitoneal glands, cholecystitis, and intestinal hemorrhage.

Regarding *pleurisy* and *pneumonia*, they have both been known to be associated with abdominal pain, the entire aspect of the case resembling very closely that of perforation. If the pneumonic process is not sufficiently near the surface to be recognizable, one can have little hope of avoiding the mistake. A careful pulmonary examination in all cases is the only possible precaution. Such cases are, however, fortunately, very rare. *Iliac thrombosis* is usually associated with sensitiveness in the groin and for a varying distance along the course of the femoral vein, and a careful examination may reveal this cause of a misleading symptom and should always be carefully kept in mind. *Appendicitis* occurring during the course of typhoid fever can very rarely be differentiated from perforation occurring in or near the cæcum, and there is fortunately no need for so doing, as the indications for operative interference are so nearly identical. *Peritonitis* without discoverable cause has been mistaken for perforation, but can scarcely give the early appearances of perforation; in either event, however, immediate interference would be indicated. *Intestinal obstruction* has simulated perforation, but here, too, the instances in which it would simulate the early symptoms of perforation must be extremely rare, while the indications for exploration would be equally certain. The considerations of consequence in connection with appendicitis, peritonitis, and obstruction with reference to perforation are not so much in relation to the difference in diagnosis, but that the conditions must be kept in mind as possible causes of the symptoms and signs in cases in

which no perforation has been found. The same may be said of cases of *suppurating mesenteric or retroperitoneal glands;* this condition can scarcely be mistaken for perforation pure and simple, but has been mistaken for resultant indications of perforation due to spreading infection. *Cholecystitis* has simulated perforation very closely, as in the case reported by Dr. H. B. Allyn, "Typhoid Fever, with Perforation of the Colon and Gall-bladder; Operation; Death; Autopsy," *Philadelphia Medical Journal,* August 3, 1901, vol. viii. p. 193. In this case no perforation was found, the existence of cholecystitis was not discovered at the operation, and the cause of the misleading indications was found only at autopsy. In such cases, however, the pain is usually high in the abdomen, and is very likely to be associated with slight jaundice or a trace of bile in the urine. Here, again, however, the important consideration is not the diagnosis, but the possibility of overlooking such a condition where no perforation is found. From *hemorrhage,* however, differential diagnosis is of the utmost importance. Less than half of the cases of hemorrhage are associated with pain, and it is probably the proportion is small in which perforation might be reasonably suspected. The diagnosis is of importance not so much because hemorrhage sometimes suggests perforation, but because the indications of perforation itself are sometimes attributed to hemorrhage, which is a mistake of the utmost gravity. Where the two conditions do suggest each other it is a diagnosis of the greatest difficulty, and in the present state of our knowledge there is relatively little to aid one. The pain and sensitiveness may be the same, the signs themselves may be almost identical. Alteration in the rate and quality of the pulse, however, may be more gradual in hemorrhage, but the difference is purely relative and not always of assistance. The evidences of systemic shock are usually more severe in perforation, but this is also a relative difference and merely a suggestion. As the case progresses the diagnosis of hemorrhage is usually rendered clear by the subsequent appearance of blood in the stools, but if perforation is strongly suspected one cannot be justified in delaying for this confirmation of the diagnosis of hemorrhage. The reduction of hæmoglobin and the number of red corpuscles, it is strongly believed, may be of material aid in differentiating these two conditions, as has been suggested by McCrae, and was of demonstrated value in one case at the Johns Hopkins Hospital. We feel that this is a most important subject, and would urge that it be widely investigated and reported for the sake of accumulated statistics. But when all is said it must be admitted that differential diagnosis between perforation and hemorrhage is sometimes extremely difficult and misleading, and in such instances one must feel justified in diagnosing perforation rather than hemorrhage, since the gravity of delay in perforation far exceeds that of exploration.

It may be well to mention here several things not already noted which may obscure or aid in the diagnosis. To one who is familiar with the not infrequent effects of tub baths, especially in severely ill cases, it would be suggested at once that the abdominal pain, muscular rigidity, and varying degrees of systemic shock sustained might lead one astray in a case where perforation was suspected or even where no such thought had been entertained previously, if the effects of tubbing were unusually marked. It is, therefore, a wise precaution in suspected cases to substitute sponge baths, in order that the diagnosis may not be obscured by ever so slight an alteration in the patient's condition from other than the suspected cause. In one of the Lakeside cases the sudden change in the patient's condition was thought to be due to the effects of the tubbing, and caused a disastrous eight-hour delay before operation. Again, in administering morphine in cases of hemorrhage one is courting danger on one hand while attempting to forestall it on the other. It is at once evident that in cases suggesting both perforation and hemorrhage the diagnosis should be clearly defined if possible before administering morphine. There are occasionally cases, however, in which one feels obliged to give morphine regardless of the consequences. One other suggestion which we have not seen mentioned elsewhere seemed at the time to be of material aid in the diagnosis in two of the Lakeside cases, in one of which perforation had actually occurred, while in the other operation was delayed and the case recovered. In both of these instances the question was raised whether the rather moderate abdominal pain might not be due to flatus. A small glycerin enema administered in each instance was expelled by both patients with the evacuation of considerable gas. In the case of actual perforation no relief from the pain was experienced, while in the case recovering without operation the pain was considerably though not entirely relieved. It is a procedure that is scarcely applicable in cases of suspected hemorrhage, but may occasionally afford information of more or less value where perforation is suspected independently of hemorrhage.

It may be permissible to consider in this connection the so-called "pre-perforative stage," upon the existence of which as an absolutely recognizable condition Dr. Cushing, of Baltimore, has been so persistently insistent. In the *Johns Hopkins Hospital Bulletin*, November, 1898, No. 92, p. 267, he defines his position as follows: "Under the 'pre-perforative' stage let it be understood that the whole period is included between the first involvement of the serosa with the customary formation of adhesions at this point, until these adhesions, which may for the time constitute the floor of the ulcer after the serosa has given way, have themselves become broken down and general extravasation has taken place." What he refers to is a pre-extravasation and not a

pre-perforative stage, and this distinction the writer himself mentions in a subsequent paper. That adhesions form in all cases of perforation is probable in spite of the fact that they cannot always be demonstrated at operation. That every case of perforation has what may be called a pre-perforative or pre-extravasation stage is too evident to need mention, just as anything that occurs has a pre-existent condition ; but when the same writer mentions it as a " definite recognizable condition " he is insisting on a refinement of abdominal diagnosis that is quite beyond the possibility of recognition with any degree of certainty. The impossibility at the present time of recognizing a distinction depending upon the thickness of the peritoneum is self-evident. An early diagnosis is the *ne plus ultra* in perforation, and doubtless in some of these cases one may feel satisfied he has found the condition mentioned by Dr. Cushing, but it is seldom to be hoped that one will strike the exact time of perforation with such accuracy. It is firmly believed that the best that can possibly be hoped for is the possibility of operating upon these cases within a considerably wider limit than Dr. Cushing urges, a little before or a little after the catastrophe has actually occurred, and the cases in which one is able to place his operation between the involvement of the peritoneum and actual extravasation are, we believe, purely fortuitous and not a matter of judgment.

Operative Treatment. It is hardly necessary any longer to urge that the treatment of typhoid perforation is solely operative. It may not be always possible to operate, but when the diagnosis of perforation is once made one can no longer consider the patient as being under treatment if operation is not employed. So far as the patient is concerned, however, it can be safely said that operation should be resorted to in all instances. This is the only reasonable ground in even the most desperate cases. The list of recoveries contains a number of the most hopeless instances of surgery as a last resort, notably the remarkable case of Dr. Abbe, *New York Medical Record*, January 5, 1895, in which operation was performed sixty hours after perforation, and in which two pints of extravasated fecal matter were removed from the abdominal cavity; also the case of Dr. Champlin, No. 155 of Dr. Tinker's series, published by Dr. Keen in his article already mentioned, in which the interval between perforation and operation was estimated at three days; and the case of Dr. Pearson, *British Medical Journal*, 1899, vol. i. p. 1097, in which recovery followed operation nine days after perforation was thought to have occurred, although in this instance there was a localized abscess about the cæcum, the case resembling more a slowly progressing appendicitis.

The *time when the operation should be performed*, that is, the number of hours after perforation, is a matter upon which statistics seem

strangely at variance with common sense and experience. Cases of perforation are always associated with a greater or less degree of shock. To operate during the severity of this condition can scarcely be considered wise unless the period of shock is unduly prolonged. The diagnosis having been made, however, the matter of an hour or two of heat and stimulation in the severest cases will serve to get the patient in as good condition for operation as one can hope. If the systemic shock is quite inconsiderable we need not delay even this length of time. If the period of shock is prolonged in spite of treatment, we believe that the danger of spreading infection will far exceed any possible benefit derived from delaying in the hope that the patient's condition will improve. It is owing to the deplorable lack of post-mortem examinations that we are obliged to assume this position instead of accepting it from demonstrated facts. The cause of death in the vast majority of reported cases has not been accurately ascertained, and where stated has been merely a clinical assumption. The number of autopsies obtainable from the reports is far too small to justify any conclusions. It is probably true, however, that general peritonitis is the cause of death in the majority of fatal cases operated upon at an early date, and in a very large proportion of cases in which operation has been delayed. It must certainly be admitted that a case dying of general peritonitis following early operation could not possibly have been saved from this catastrophe by delaying a number of hours. The statistics of Dr. Westcott and Dr. Tinker, published by Dr. Keen, show that the largest percentage of recoveries follows operations performed during the second twelve hours after perforation. We cannot but feel, however, that these statistics, convincing as they first appear, are quite misleading. They are largely made up of the older cases, in most of which operation was long delayed and among which the recoveries were largely instances of fortuitous and unlooked-for good fortune. The fact, also, already mentioned, that the cause of death in all but a few of these cases was never definitely known affords a possibility of error that renders the statistics practically useless. In the more recent cases recovery has been much more frequent among those in which operation was early peformed. But even here, again, unless sufficient interest is exercised to demonstrate positively the cause of death in unsuccessful cases, the decision of this question must be largely a matter of general experience and not scientific demonstration.

The nature of the *anæsthetic* will often prove to be a matter of consequence, especially whether one will employ local or general anæsthesia. There are frequently serious objections to both, but we cannot at all subscribe to the feeling of certain writers who claim that local anæsthesia should be employed in all cases, and that the use of general anæsthesia is a deplorable mistake. By the employment of local anæs-

thesia it has been thought to obviate entirely the additional shock of the administration of a general anæsthetic. In some instances this is so, in others it is purely an assumption. It is too often the case that what may be spoken of as purely operative shock is largely attributed to the use of a general anæsthetic, and no one will maintain that laparotomy under cocaine, in which the abdominal contents are disturbed, is entirely relieved of shock by the omission of a general anæsthetic. The mental anxiety, worry, and dread incident to a laparotomy under local anæsthesia in a hardy, strong individual, or even in a patient whose sensibilities are dulled to no inconsiderable degree by the severity of the illness, is a consideration never to be overlooked and will not infrequently render the decision against local anæsthesia. What is to be accomplished is the greatest possible reduction of systemic shock to the patient incident to the operation, and in some instances this is best accomplished by local anæsthesia, in others by general anæsthesia. Stolid and more or less apathetic patients are more favorable for local anæsthesia. The amount of self-control an individual is able to maintain is a very uncertain indication, as the greatest self-control may sometimes be associated with extreme and very depressing mental strain. Even in those cases in which a local anæsthetic has been properly and successfully employed, it is doubtful if the extensive and careful abdominal irrigation usually required, can be as well accomplished in most instances without resorting to a general anæsthetic at this stage of the operation. As so much depends on the care and thoroughness of this part of the procedure, it does not seem always wise to complete it under local anæsthesia unless the indications are very direct.

One of the main objections to general anæsthesia is the fact that so much time is usually lost in getting the patient sufficiently under. This may be obviated by using chloroform after the administration of about one-quarter grain of morphine hypodermically; but what we feel will eventually prove a still more rapid and considerably safer method is the employment of nitrous oxide and oxygen followed by ether. By using the gas and ether alternately in getting the patient under, complete anæsthesia can be produced readily in one to two minutes, and the method is devoid of the unforeseen but ever-present dangers incident to chloroform. The prolonged use of nitrous oxide and oxygen alone may eventually displace the use of chloroform and ether altogether in these cases, but at the present time its usefulness and safety for prolonged anæsthesia has not been sufficiently demonstrated. When general anæsthesia is employed it is unnecessary to add that it should be given into the hands of one of very considerable experience, and the administration should be as light and as short as possible. One advantage of the general anæsthetic thus administered over local anæs-

thesia, which we feel is not always kept in mind, is the greater rapidity with which the operation can be done under general anæsthesia, and the considerable reduction of the exposure and handling of the patient, to say nothing of the added thoroughness with which the operation may be performed. The use of local anæsthesia in these cases is an extremely simple matter to one who has even a limited abdominal experience, but its usefulness and employment is something which should be carefully considered and not entirely assumed.

The requirements of operation are so direct and clear that the *technique* is simple, and the steps of the operation well defined and logical. As an operative procedure it has been so well developed that we can look for comparatively little improvement in this direction, and there is consequently much less of interest in this portion of the discussion. The *incision* in the right lower quadrant of the abdomen is the only logical opening in these cases, and the linea semilunaris opposite or a little above the anterior superior spine we believe to be preferable. The lower part of the ileum, the cæcum, and the appendix include the vast majority of perforations, and are, on the whole, most readily accessible through the incision mentioned. An additional advantage of this incision is the well-recognized fact that the search for perforation is best begun from the cæcum. The incision should be sufficiently generous, perhaps 8 to 10 cm. long, to allow a careful and somewhat visual exploration. It occasionally happens that the perforation is completely protected by well-formed adhesions and fecal extravasations prevented, as was the case in an operation performed by Dr. J. C. Warren, reported by Dr. R. B. Greenough, *Boston Medical and Surgical Journal*, May 8, 1902, vol. cxlvi. p. 491. If these adhesions are blindly broken up through a small incision unnecessary fecal extravasation may occur, the danger of which, owing to the certainty of the infection, cannot be estimated.

After entering the abdomen the first *search for the perforation* should be made in the ileum immediately above the cæcum, as the vast majority of perforations occur in this portion of the gut. By far the best way of accomplishing this is by starting at the cæcum, a fixed point very quickly found. We feel that this is a very wise routine procedure to employ, since one knows accurately the exact location of the small intestine he is handling and avoids the discouraging loss of time almost invariably incident to a haphazard and undiscriminating inspection of coils of small intestine appearing in the wound. Starting with the cæcum, one should inspect the ileum for a distance of about one metre. There is no object in going above this unless one intends to search the entire intestinal tract. This search for the perforation can be hurriedly but carefully conducted if the incision is sufficiently large to afford even a limited view of the general field. It is usually con-

sidered wise to replace the coils of intestine within the abdomen as the search is made, although some feel, and not without reason, that keeping the explored portion of the intestine well covered with hot towels and finally replacing all the coils at once can be accomplished with less handling of the intestines and less incident shock to the patient. We feel it is wise to make this first hurried search of the ileum for the perforation only, which is immediately recognized if present, a more careful examination of the gut for very thin ulcers being made after the really serious features are corrected, providing the condition of the patient will permit. It also affords a comprehensive conception of the portion of the bowel almost invariably affected, and prevents the possibility of spending valuable time over relatively unimportant conditions. It is, therefore, well to make this entire rapid inspection of the bowel even before closing any perforation that may be found. It is a very simple matter for an assistant to retain the location of these perforations outside the abdomen with sponges. The *method of closure of the perforation* is relatively unimportant, but should always be done with silk; catgut alone has been demonstrated on several occasions to be insufficient. A short double row of continuous Lembert sutures is all that is required, and can be very rapidly placed without elaboration. Excising the ulcer before suturing is an utterly useless and time-consuming procedure. It is a rare exception to find an ulcer of such size that the suture encroaches to an important degree upon the lumen of the gut; in such instances the suture must be placed with greater care. If there are several neighboring or confluent perforations, or the integrity of a considerable portion of the gut is severely impaired by deep ulcerations not yet perforated, it is wise to secure this portion of the intestine to the edge of the wound rather than consume time by resection or an elaborate method of suture, and to close the fistula subsequently. Having secured the perforation, if the condition of the patient permits, it is always wise to make a retrograde search of this last metre of the ileum for *deep ulcerations threatening perforation.* These can be recognized with considerable accuracy by the trained touch. Running the finger down over the bowel the dangerous areas are indicated by small, soft, circular places in the centre of a moderately large, thickened area. The sensation is readily acquired by post-mortem examination of an ulcerated ileum, in which the observation can be verified by subsequently opening the bowel. These areas when found should be reinforced by a running silk Lembert suture. The cæcum and appendix being immediately at hand, it is well to give them a passing inspection. One is scarcely justified, however, in removing the appendix unless it is seriously affected, and not in instances where it is "at all abnormal," as was recommended by Dr. Finney, in his article in the *Johns Hop-*

kins Hospital Reports. If no perforation has been found in the search so far instituted, it is inadvisable to make further examination of the intestinal tract, excepting, possibly, the sigmoid flexure, which is occasionally, though quite rarely, affected. Typhoid perforations in other locations are so extremely rare that one would lose many more patients in a prolonged intestinal search than in running the slight risk of having overlooked such a condition.

Irrigation of the abdominal cavity we feel should be somewhat prolonged and very thorough, even if there are no visible evidences of peritonitis or extravasation. The stimulating usefulness of hot irrigation has been even urged in explorations where no perforation has been found, but at the present time one hardly feels inclined to irrigate in such cases. In many instances this abdominal irrigation should be deferred until the inspection of the gut has been made, unless the inspection is seriously hindered by the amount or nature of the fluid present, in which case a rapid preliminary irrigation may be useful, the main irrigation, however, to be reserved until after the treatment of the bowel. Salt solution is possibly preferable to sterile water, but either one will do. It should be about 115° F., copious in amount. This, we feel, is best and most wisely accomplished through one or several irrigating tubes without removal of the intestines, and should be especially thorough in the region of the pelvis and lumbar fossæ. It is often well to irrigate the pelvis first, introducing a large rubber tube which will take up a large part of the return flow; in this way one will not infrequently avoid general dissemination of a large proportion of the abdominal fluid and fecal extravasation which very frequently settles to the pelvis. If extensive peritonitis is already present, one must treat this complicating incident as such, and that will vary greatly according to individual belief. We feel, however, that the extensive intestinal manipulation sometimes advised in such cases is of doubtful wisdom unless the condition of the patient is unusually favorable. We would feel inclined to rely on thorough and prolonged irrigation of the abdomen without removal of the intestines, as this is about all such patients can endure. In many instances, to properly accomplish this irrigation to the best advantage, we feel that a general anæsthetic is advisable, although it is occasionally satisfactorily accomplished under local anæsthesia.

It may seem occasionally wise to close these cases without *drainage*, but such has certainly been felt to be the rare exception. It is possible that having the temerity to close these cases after thorough irrigation may add considerably to the recovery rate; such cases, however, should certainly be restricted to those in which examination of the abdominal fluid during the operation shows the absence of organisms, or, possibly, those in which only bacilli are found to be present; but

the advisability of drainage is scarcely questioned at the present time. The way in which one drains will vary according to the operator's personal belief. Whatever the method, however, it seems advisable to drain the pelvis. In the Lakeside cases what proved to be a very satisfactory method was by means of glass drainage tubes leading to the pelvis, and along the side of the tubes in some instances gauze drainage was also placed. It seems wise, also, to leave the seat of perforation or doubtful portions of the bowel near the incision, introducing gauze drainage to this portion of the bowel in order, if possible, to forestall the disastrous consequences of insecure suture or subsequent perforation. Around the drainage the wound should be closed as completely as possible, as the granulating capacity of such patients is sometimes considerably reduced, although the healing of wounds by first intention seems to be rapid and secure.

While it is needless to say that the operation should be done as rapidly as possible, it must still be remembered that *these patients bear operation* much better than one would ordinarily be led to suppose who had not had the opportunity for personal observation. The incision, the search for perforation, the repair of the bowel, can all be very rapidly and at the same time thoroughly performed, so that this portion of the operation may well be considered the minor part. The careful and thorough irrigation, however, is a matter that cannot be unduly hurried, although here the time can be somewhat diminished by having several irrigating tubes in use at the same time. This portion of the operation, while possibly consuming the most time, is the least depressing to the patient, as it is associated with a considerable degree of stimulation. We fear not a few cases are sacrificed through lack of proper irrigation, owing to the overwhelming desire of operators to complete the operation in as short a time as possible. We would urge the desirability of the utmost speed during the really operative part of the procedure, which is easily possible for any operator of moderate dexterity and good judgment, but would deprecate hurried and inadequate cleansing of the abdominal cavity. The superior ease and rapidity with which one can accomplish the operation under a general anæsthetic is often in marked contrast to the slow, painstaking procedure not infrequently required under local anæsthesia where the sensibilities of the patient are so keenly alive to what is going on, and this consideration, as previously mentioned, will not infrequently incline the operator to the use of general anæsthesia as of marked advantage.

The *subsequent treatment* of these cases presents nothing distinctive or striking, it only being necessary to keep in mind the requirements of the patient from the standpoint of a laparotomy on the one hand and that of typhoid infection on the other. While we do not mean to sug-

gest that the treatment of such cases does not require the greatest care and judgment, it presents no distinctive feature which need be dwelt upon. One thing, however, is extremely desirable, namely, to keep constantly in mind the possibility of a subsequent perforation, and avoid as far as one is able the possibility of obscuring the manifestations of this occurrence in any way by the line of treatment.

The question of *exploratory incision* in rather doubtful cases of suspected perforation we feel is a matter of great importance and increasing interest. This has been most advantageously urged and considered by Dr. H. W. Cushing, and is, we feel, his most useful contribution to the surgery of these cases. It has been exceptionally well expressed in his article, " Sur la Laparotomie Exploratrice Précoce dans la Perforation Intestinale au cours de la Fièvre Typhoide," *Archives Générales de Médecine*, January, 1901. In instances where perforation is suspected, but the diagnosis cannot be considered as definitely made, exploration affords the only hope of avoiding the catastrophe of allowing a perforation to go unrecognized until more or less general infection has occurred. Even at the present time it has been proven beyond a reasonable question that these operations when properly performed are practically devoid of danger and affect the condition and course of the patient to a scarcely appreciable degree, whether performed under local or light and rapid general anæsthesia. If no perforation is found the abdomen can be immediately closed, a collodion dressing applied and the baths resumed within a few hours, so that treatment of the patient need scarcely be interrupted. Such was the case in No. 4 of the Lakeside series. The impervious dressing necessary for continued tubbing is conveniently applied by using six or eight alternate layers of collodion and sheet wadding, each layer being a little larger than the one previously applied. It is well to use only half of the thickness of the ordinary sheet wadding.

Exploration was first suggested by Dr. Finney, who advised making a very minute incision for the purpose of taking cultures from the abdominal cavity. This method was employed in the Lakeside case mentioned, but the restricted nature of this exploration was considered a mistake, and can certainly be no longer recommended. One must now be able to detect more than the presence of free abdominal fluid or organisms within the abdominal cavity. The perforation may be protected by adhesions or the ulceration may be scarcely through the peritoneum, either of which conditions may occur without being discovered by such restricted exploration. If one is to look at all he should examine the ileum and cæcum with care; it will take scarcely more time and will afford information of consequence. It must be readily admitted that the very slight danger incident to a rapid, skilful exploration is not to be compared with the serious consequences of an

unrecognized perforation. Considering this as an aid to diagnosis, it is largely along this line that we are to look for a considerably larger percentage of recoveries from perforation. It will necessarily result occasionally in a premature operation, but will add very materially to the number of lives saved.

In instances where no perforation is found, either with or without evidences of peritoneal infection, at once arises the question of how far one may feel justified in exploring the abdomen for such *other intra-abdominal conditions* as have been known to suggest perforation. This is a matter which will be decided entirely by the individual judgment of the operator, and must be affected to a greater or less degree by the condition of the patient. Where, however, one finds an abnormal intra-abdominal condition, as peritonitis, for instance, it seems hardly justifiable to limit the search for the seat of the trouble to a rapid glance at the ileum and cæcum. The appendix is so close at hand that its inspection should never be omitted. The detection of suppurating mesenteric glands is important for the sake of adequate disposition of drainage. Exploration of the region of the gall-bladder may be accomplished without serious objection. The presence of intestinal obstruction may possibly be detected by a hurried examination of the intestine from several parts of the abdomen. Unless the indications are pretty direct, however, one would scarcely feel inclined to risk much time on this very remote possibility. The extent to which these explorations are to be pushed is a matter for much thoughtful consideration.

The advisability of *secondary operation* for subsequent perforation or other operative indications is no longer a matter of general question, but of individual judgment in each case. The remarkable vitality displayed in a number of reported cases in which two or more subsequent operations were performed, has established this point beyond reasonable question. Operative indications are to be followed, and can no longer be set aside, for the simple reason that the patient has already undergone one operation.

Prognosis. At the present time it is extremely difficult to form even a reasonable idea of the prognosis in these cases. We know that it is affected by a number of conditions. In general, the recovery rate is higher among young people. The time during the disease at which perforation occurs has an influence, since the recuperative powers of the individual are altered at different times. Recovery is less frequently to be expected when perforation occurs during the height and severity of the disease, whether of a primary attack or in the midst of a severe recurrence. When perforation occurs early in the disease, before the vitality of the patient has been drawn upon to any considerable degree, the prognosis in general is better, and also during conval-

escence after the recuperative powers of the individual have begun to assert an advantage. The prognosis is always severely affected, of course, by the length of time the case has been allowed to go after perforation, the extent to which a spreading abdominal infection has occurred, and the bacterial nature of this infection. It is also largely affected by the judgment, skill, and dexterity of the operator. But when it comes to an estimation of the percentage of recoveries the figures obtainable from the present statistics are, we believe, absolutely unreliable. In Dr. Westcott's table, comprising the first 83 cases reported, the recovery rate was 19.3 per cent., while in Dr. Tinker's table, comprising, presumably, the next 75 cases reported, the recovery rate was 28 per cent., making an average recovery rate for the entire 158 cases of 23.41 per cent. This recovery rate is far below that obtainable under the present conditions of diagnosis and operative technique; but the prognostic suggestions afforded by even the most recent cases which the writer has carefully collected are, we feel, too inaccurate and undiscriminating to deserve mention. This analysis affords a certain percentage of deaths associated with operation, to be sure, but many of the cases dying after operation bear no relation whatsoever to the true mortality in direct connection with either the perforation itself or the operation. This last statement has been most satisfactorily demonstrated by several post-mortem examinations in the Lakeside series. With but rare exceptions it has been impossible to draw this distinction in our study of recent cases owing to the incompleteness of the reports, but we are sure such a discrimination would alter materially our statistical mortality. Dr. Osler has divided these cases into three classes: those which recover from operation, those which die from causes immediately related to perforation and operation, and those which die from causes entirely unrelated to either. It is of the utmost importance that this distinction be kept closely in mind in forming an estimate of the mortality in these operations, but it is a distinction which, curiously enough, seems to have almost entirely escaped the thought of those attempting to form a statistical opinion of recovery and mortality. It is absolutely impossible to acquire the knowledge necessary to form this more accurate opinion without wide and accurate pathological observation and careful post-mortem examinations. An attempt was made by the writer to form such an estimate from the number of autopsies reported, but the number at present is so small and the reports are so fragmentary and inaccurate that the analysis has proved utterly worthless. Unless the operators under whose observation these cases are occurring can contribute generously to our pathological knowledge, any further reports are practically useless and might much better be omitted, since superficial reports only burden the literature without contributing to our present knowl-

edge. Dr. Keen estimates that we can look forward to 30 per cent. of recoveries. The recovery rate at the Johns Hopkins Hospital of cases occurring while under treatment in the wards is 45.4 per cent. Dr. Osler estimated a possible recovery rate of 50 per cent., and Dr. Cushing of 50 to 60 per cent. We cannot but believe that a discriminating analysis in well-observed cases with complete pathological examinations would give a recovery rate considerably in excess of this, possibly 70 per cent.

Pathological Considerations. The *nature of the abdominal infection* in these cases is purely fortuitous, being drawn from the wealth of bacterial flora of the ileum, the possibilities of which have probably never yet been exhausted. The proportion of cases in which bacterial examination of the abdominal fluid has been made is very small, but such examinations have been more frequent in recent cases as their usefulness and prognostic value have become more evident. The infections as a rule, however, appear to be mild, largely bacillary, bacillus coli communis and bacillus mucosus capsulatus being the most frequent. One strange incident of a pure infection of staphylococcus pyogenes aureus has been reported. Some half-dozen cases of infection with bacillus typhosus have been collected, from which it appears that these cases are attended with a high mortality. It will be necessary, however, to have a large number of cases in which a complete and careful bacterial examination has been made to give these results anything more than a passing interest. It is very desirable that our knowledge of the nature of these infections be widely increased, as it may eventually be found that certain features in the treatment can be altered to advantage according to the nature of the infection. It is possible that certain infections which are recognizable from cover-slip examinations will require very much less thorough irrigation, for instance, and that in some cases we are at present subjecting the patient to a considerably more severe strain than the circumstances may require. Cover-slips and cultures should be freely taken, and as these procedures require but a moment they need scarcely interfere with the rapidity of the operation. These examinations should be made not only from the fluid first encountered on opening the abdomen, but also from the lower and more dependent levels, as it sometimes happens that the upper part of the abdominal fluid appears to be free from organisms, and one is led to the erroneous conclusion that no bacterial infection has occurred. It is very desirable, also, to make an examination from the site of the perforation itself, and this, of course, is especially necessary in early cases where no appreciable amount of abdominal fluid is present.

It has been thoroughly demonstrated pathologically, and in several instances has apparently been clinically confirmed, that *infection of*

the peritoneal cavity may occur through the base of an ulcer without perforation, or even through the inflamed portion of the intestine itself without deep ulceration. Such a case was reported by Dr. Ioison, "Du Traitement du Chirurgie de la Péritonite Suppurèe Diffuse," *Revue de Chirurgie*, February 10, 1901, No. 2, where no solution in continuity of the bowel was found either at operation or autopsy. It is extremely probable, also, that such was the condition in the case of Dr. Dandridge, No. 28 of the Westcott series, in which no perforation was found, but the abdomen contained gas and free pus. The patient was irrigated and drained, and recovery followed. Such instances, however, are quite unusual, and it is hardly safe to assume that the case is of this variety, simply because no perforation is found in the rapid search of the ileum. It is, we feel, rather safer to assume that infection has occurred from some other source, which should be found and corrected as circumstances may permit.

It is probable that *adhesions* more or less extensive occur in all of these cases and that the infrequency with which they are reported is due to inaccurate observation necessitated by a very restricted incision through which the bowel has been drawn before the examination was made. As mentioned above, this procedure does not seem wise, since adhesions forming a perfect protection for the peritoneal cavity against infection may be blindly broken up and the opportunity offered for general infection. It is not meant in recommending a rather more generous incision that there is a necessity for actual visual observation of the entire field, but that by this means sufficient care can be exercised in the withdrawal of intestine to prevent fecal extravasation and infection where such has not yet occurred. In cases of what appear to be sudden perforation it is doubtful if these adhesions are of sufficient consequence to afford much protection. In the Lakeside cases, while no adhesions were found in those operated upon for perforation itself, it was probably true that they were overlooked through insufficient care in the search for the lesion.

With reference to the *great practical value of complete postmortem examinations* in these cases, too much cannot be said. The greatest interest thus far seems to have centred in reporting certain clinical features and the circumstances of recovery, and from the small number and paucity of the postmortem examinations it is evident that very little interest has been taken in this part of the subject. It is perfectly useless to continue reporting simple recoveries for the sake of apparently increasing the recovery rate. What is most essential at the present time is a large collection of well-observed and well-reported autopsies. A complete examination, however, does not necessarily mean a complete autopsy. Through even a restricted incision it is possible to gain a fairly accurate conception of the extent and nature of

the peritoneal infection if present; the appearance of the bowel for the sake of comparison with that observed at operation; the presence of additional perforations, overlooked or subsequent, and the existence of threatening perforations; the degree of success with which the suturing has been accomplished, and other respects in which the operative technique has been unsuccessful. Cultures may also be widely taken through such an incision, and the spleen, heart, and lungs examined. Blood cultures should also be taken. It is only in this way that we are going to be able to arrive at some definite conclusions as to the cause of death in these cases and the respects in which the treatment has been unsuccessful, and it is only by these means that the mistakes that are constantly being made in every case of perforation, either in diagnosis or treatment, can be rectified. For the sake of the present patients the clinical features and the operation are of sole consequence; the interest of future patients, for the present at least, lies almost entirely in pathological examinations.

In the apparent hope of giving some general direction to the clinical features of these cases, Dr. Osler has published the specific instructions which are followed in the medical wards at the Johns Hopkins Hospital, "Perforation and Perforative Peritonitis in Typhoid Fever," *Philadelphia Medical Journal*, January 19, 1901, vol. vii. p. 116. This is as admirable a schedule as can well be imagined, and could most profitably be adopted for the sake of complete and uniform observation. To this schedule we would feel inclined, from an operative and pathological standpoint, to add certain suggestions which may be an aid in determining with more accuracy some of the unrecognized features mentioned in connection with these cases. Doubtful clinical features of so much consequence in establishing the all-important early diagnosis are covered by the Hopkins schedule. For the sake of a general and more accurate idea of the amount of systemic depression associated with the anæsthetic, the operation, or both, it is well to note with as minute accuracy as possible the condition of the patient immediately before and immediately following operation, as well as the changes in his condition for at least twenty-four hours subsequent to the operation. In taking cover-slips and cultures these should be obtained from various parts of the abdomen and also from the upper and lower portions of the abdominal fluid if present, and from the site of perforation. It is desirable to note with much care the general condition of the bowel, the nature and extent of adhesions, and the extent and severity of the general infection if present, for the sake of comparison with post-mortem examination in case the patient does not recover. In the post-mortem examinations, whether complete or restricted, the condition of the bowel and the extent of infection should be carefully noted; cover-slips and cultures should be widely taken

from the abdomen, organs, and blood; the condition of the operative field in the bowel should be carefully observed, also the presence of additional perforations, either those overlooked during the operation or those apparently subsequent to the operation, and the presence of threatening perforations. These are all points of special consequence, which, it is believed, will lead to an accumulation of facts of much practical value if carefully and generally observed. It is necessary to make so many of these post-mortem examinations without the direction of a trained pathologist that the circumstance seems to justify the mention of these details. It is from well-equipped hospitals that we must first look for such a class of reports, as elsewhere it is scarcely possible to have both medical and surgical observation of all typhoid cases, and especially of all suspicious cases. A means which will add very materially to the unity and usefulness of these observations and reports, and which will tend to develop a degree of judgment in diagnosis and operation that cannot possibly be obtained in any other way, may be afforded by having all these cases brought under the immediate control of one member of the hospital staff. The number of perforations occurring during a year in any one institution is not large, and if the opportunities for observation and treatment are divided among a number of men the experience gained by each is very limited, the observations are very apt to be restricted and unmethodical, and the combined judgment rather biased and uncertain according to the nature of the particular case or two which has come to the hand of any one man. We feel that if this suggestion could be carried out our knowledge of this subject would be widely, rapidly, and very beneficially increased.

While, however, it is true that a large portion of these operations will still be done in hospitals, mainly on account of the difficulties in diagnosis, it is still interesting to note that there has been reported by a general practitioner one successful case in a country house under the conditions which one finds there ordinarily existent. The case was reported by Dr. R. T. Davis, "Perforation in Typhoid Fever; Operation; Recovery," *American Medicine*, January 18, 1902, vol. iii. p. 116. The operation was performed only six hours after perforation was thought to have occurred, which betokens a degree of watchfulness that one can scarcely hope to obtain with much frequency under such conditions. As this is the first case of its kind reported it is of special interest in showing the changing attitude of the medical profession in general with reference to perforation during the course of typhoid fever.

SOME PHASES OF GALLSTONE DISEASE, WITH SPECIAL REFERENCE TO DIAGNOSIS AND TREATMENT.

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The dominant factor in the formation of gallstones apparently is bacterial invasion of the gall-bladder plus a tendency to stagnation of the bile in that viscus. It was formerly thought, since normal bile is usually sterile, bacteria could not thrive in that fluid; but it is now established that bile is a fertile culture medium for many varieties of pathogenic bacteria, notably the Eberth bacillus and the colon bacillus and its varieties, which may assume pathogenic properties.

The bacteria most commonly found in connection with cholecystitis and gallstone formation are the colon and typhoid bacillus, and, less commonly, the gall-bladder is invaded by streptococci, staphylococci, and the pneumococcus.[1]

The invasion of the gall-bladder by bacteria occurs either by the blood (portal vein, thence eliminated by the liver in the bile), the likely mode of the almost invariable infection of the gall-bladder in typhoid fever, or through the duodenum by means of the common bile duct and the cystic duct, the probable source of colon bacillus infection.

With the latter mode of entry the infection may and often is a mixed one, since the healthy duodenum is said to normally harbor not only the colon organism, but also staphylococci and streptococci. It seems established, as just remarked, that in nearly all, if not in all, cases of typhoid fever infection of the bile by the specific micro-organism occurs. It is interesting, such being the case, that in only a limited number of these does cholecystitis immediately or subsequently develop, or are pathological changes in the walls of the gall-bladder found in cases of lethal typhoid.

Bacteria do not normally readily migrate into the bile passages from the intestines, and the pathological condition which favors their entrance is somewhat similar to that which favors, by their aid, gallstone formation—stagnation in the outflow of bile through the ducts. Obtaining an entrance into the gall-bladder, these organisms probably lead to the formation of gallstones in the manner originally suggested by Naunyn, by inducing a catarrh of the gall-bladder through infection of its wall; or even without such an infection the formation of

[1] For details of this part of the subject the reader is referred to the article by Pratt, Typhoid Cholecystitis, with Observations upon Gallstone Formations, The American Journal of the Medical Sciences, November, 1891; and that of Richardson on the Bacteriology of the Gall-bladder, in Warren's Surgical Pathology and Therapeutics.

calculi may be promptly favored by virtue of the acid production of such organisms as the Eberth and the colon bacillus. This acid production leads to precipitation of bile acids and of cholesterin. Stagnation of bile occurs in the gall-bladder, whence result concentration, and subsequently, through cholesterin, bile acids, and bilirubin-calcium precipitation, stone formation is readily induced.[1]

Micro-organisms have been found in many instances of fairly recent stone formations in the very centre of the stone, as if they had been an original portion of the nidus; and in gallstone formation in recent subjects of typhoid fever experimental evidence indicates that the Eberth bacilli, clumping in the gall-bladder, may offer nidi for precipitation of cholesterin and other products entering into the composition of biliary calculi.

A cholecystitis recognizable other than by minute pathological changes in the wall of the gall-bladder is not an essential factor in gallstone formation.

Cholecystitis is more common in women than in men, and is still more usual in childbearing women (of 115 women gallstone subjects, 99 had borne children—Naunyn). The frequency of the affection increases with age. This preponderance of frequency is evidently related to increased bile stasis, resulting from the relatively less respiratory activity in woman than in man, in the pregnant woman than in the nullipara, and in the aged than in the young.

Cholelithiasis is a very common condition. Riedel (quoted by Kehr) holds that in Germany nearly 10 per cent. of the adult population are gallstone subjects. This percentage is probably much greater than exists in Great Britain or in the United States. It is interesting and important that but a relatively very small percentage of those with gallstones ever have symptoms suggesting their presence. Kehr believes that approximately 95 per cent. remain free from symptoms; but this estimation is probably much too high, as many cases of minor transient and infrequent attacks of colic due to mild cholecystitis occur in those who never consult the physician or in whom these transient colics are wrongly diagnosed. However this may be, this infrequence of symptoms is a suggestive fact and indicates what seems now well established, that something other than mechanical irritation of the stone is required to induce the symptoms whereby the presence of calculi is recognized.

Cholelithiasis is usually latent until a reinfection of the gall-bladder determines the condition manifesting its presence.[2] If, with stone

[1] Frerichs long ago held that gallstones originated as the result of bile stagnation, the mucus secreted by the gall-bladder favoring an acid reaction of the bile, with consequent precipitation of its salts. He was, of course, unaware of the rôle bacteria played in the formation of calculi.

[2] Cholecystitis may occur primarily without the presence of stone, as in the acute infection of the gall-bladder in typhoid fever and in pneumonia.

formation, the infection of the gall-bladder has not given rise to other than minor and transient pathological changes in the walls of this viscus, and adhesions are absent and the cystic duct patent, only in exceptional cases is it likely that attempted extrusion of a stone occurs. Symptoms incident to the latter commonly originate from a cholecystitis dependent upon reinfection, either newly acquired or from a pathogenic micro-organism, long latent in the gall-bladder, perhaps the original source of the calculi. There are many instances on record of typhoid cholecystitis occurring primarily a number of years after the original attack of typhoid fever.

While mechanical irritation of the stone itself rarely originates biliary colic, it is, of course, probable that in conditions favoring stagnation of bile in the gall-bladder and prolonged distention of that viscus, such as would be induced by muscular inactivity and fasting, that transient colics occur in gallstone subjects, without a coincident cholecystitis. Usually frank attacks, or those of mild, ephemeral nature, if tending to recur, indicate infection of the gall-bladder, with its resulting inflammation. The symptoms of recognizable cholelithiasis are, therefore, usually those of cholecystitis or one or more of the latter's complications, such as pericholecystitis (adhesions), obstruction of the common bile duct, or cholangitis.

The most common form of cholelithiasis encountered is that associated with catarrhal inflammation of the gall-bladder, the result usually of a moderate grade of infection. In this there is often an abortive attempt at passage of a stone, and the stone may engage the neck of the gall-bladder or lodge in the cystic duct. The infection is transient and its degree mild. There may occur a so-called dropsy of the gall-bladder of either minor or major degree, but ephemeral almost in duration, if obstruction of the duct by a stone does not exist. In any event, with infection of mild degree and transient, the symptoms are of brief duration unless the calculus passes into the common duct, and there lodging, temporarily or permanently, by interfering with the outflow of bile, causes the usual phenomena of obstruction with jaundice. This last is the form of gallstone colic alone usually recognized by the general practitioner. With a high grade of infection, and either with or without a patent cystic duct, empyema of the gall-bladder may develop either immediately or subsequent to simple dropsy of its cavity. Empyema may occur coincident with a primary attack of hepatic colic, or after repeated seizures, with more or less long intervals of repose. If the calculus has entered the common duct, the infection continuing, there may result diffuse inflammation of the smaller bile ducts, or cholangitis.

A frequent accompaniment of repeated attacks of calculous cholecystitis, is pericholecystitis, resulting in the formation of adhesions

between the gall-bladder and contiguous structures, such as the omentum, stomach, or intestines.

Apart from perforation of a gall-bladder the seat of a recent empyema with frank symptoms, a not rare effect of latent cholelithiasis with adhesions, is perforation of the gall-bladder or of one of the bile ducts harboring a calculus, with passage of the latter into a contiguous adherent organ, such as the bowel or stomach, the first recognized indication of gallstone being the voiding of the calculus by the bowel or an obstruction of the lower part of the ileum by the stone too large to pass the ileocæcal valve.

As a more remote but not uncommon effect of gallstone disease there may result dilatation of the stomach from adhesions about the pylorus or duodenum constricting its outlet; recurring gall-bladder colics even without presence of stone from similar adhesions, and gastralgia and enteralgia similarly arising. In addition to the numerous ill effects from adhesions, other not unusual remote results of gallstone disease are carcinoma of the gall-bladder, or of the common duct, or of the head of the pancreas. Hepatic cirrhosis from continued occlusion of the common duct, interstitial pancreatitis and acute hemorrhagic pancreatitis, and pancreatic fat necrosis are among the complications or more remote effects.

Catarrhal calculous cholecystitis is not only very common, but, as before remarked, is frequently improperly diagnosed. My attention was first forcibly directed to this fact long ago by some remarks of Jonathan Hutchinson.[1] In then discussing a paper by Dr. Ord concerning the more rare symptoms produced by gallstones, Mr. Hutchinson referred especially to these slight passing attacks of colic which were commonly regarded to result from stomach disorder, but in reality were due to spasm not of the stomach, but of the gall-bladder. He spoke of the importance of an inquiry for a history of such attacks in the past in arriving at a diagnosis, when later in the case more pronounced symptoms suggestive of the presence of gallstones occurred. He dwelt on the necessity of careful inquiry for symptoms which may have been regarded as too trivial to mention, and on the necessity for examination of the gall-bladder region, and emphasized the mistake so often committed by the physician in viewing jaundice as essential to the diagnosis of cholecystitis. He remarked: "Hepatic colic is a far more common event than it is generally supposed to be, and many cases escape recognition because there is a general belief that jaundice ought to be present."

This statement of Hutchinson impressed me very forcibly at the time of its publication, and caused me to be on the alert for such cases,

[1] British Medical Journal, June 30, 1888.

and in the past fourteen years has been very helpful in their recognition. I have seen many that might have been viewed as simple gastralgia and as cases of recurring gastritis that were unquestionably calculous cystitis. Certain of these cases have been of a very mild type; there has been little or no rise in temperature noted, and the colic recurring irregularly at intervals of a few days is unassociated with a palpable gall-bladder. The pains, too, are often referred solely to the epigastrium, but examination may show the gall-bladder region to be acutely sensitive during the seizure, with frequently a continuance of the sensitiveness in less degree for some time after. It is especially important to be on the watch for such cases, since in certain of them in which obstruction of the duct has occurred, with resulting hydrops, empyema of the gall-bladder may develop very insidiously.

A case of mild recurring, probably calculous, cholecystitis is now under observation in a woman, aged thirty-six years, who, apart from attacks of what she presumed to be stomach spasm, has always been in good health. The first attack occurred four years ago, and, she thought, had been induced by eating when over-fatigued. The second attack occurred seven months later, and following this they recurred about twice a year until two years ago; then their frequency increased, a seizure appearing at intervals of two or three weeks, until I saw her one year ago. The attacks occur suddenly without premonitory warnings, and bear no definite relation to the time of meals or character of food eaten. Severe pain appears in the centre of the epigastrium and to the right. The seizures have occurred through the night on three occasions only. She thought they were more usual before the menstrual period.[1] There are no special dyspeptic symptoms save, following the attacks, flatulency. The tongue is clean and the bowels regular. Vomiting is not unusual before the seizure. The attack often lasts an hour or two, and is dissipated by hot applications and the ingestion of cajuput oil in spirits of chloroform. The patient is of full habit and is very fond of sweets, and takes little exercise. Examination showed slight gastroptosis; gastric motility normal; diminished secretory activity. Examinations in the intervals disclosed slightly palpable, sensitive gall-bladder; no sensitiveness elsewhere in the abdomen. Palpation of the gall-bladder region, although carefully done, was followed by extreme soreness persisting for several days. The patient was subsequently seen once during a seizure when, although the gall-bladder was not palpable, there was marked tenderness in this region. This patient had been treated for simple gastralgia until I saw her. Stones probably at no time were voided; the attacks were of too short duration to suggest this, and jaundice has never occurred. The patient has had no seizure since the first few months of treatment. Gallstones were persistently searched for in the stools.

An interesting case recently seen of dropsy of the gall-bladder is the following: Mrs. H. H. S., aged fifty years. In September, 1901,

[1] It is a fact that the occurrence of pains of this sort is more common at this time, probably for the reason that, as mentioned by Kehr, the portal viscera, then more surcharged with blood, are more subject to inflammatory reaction.

the patient, while driving, was seized with severe epigastric pain and vomiting. The pain continued irregularly for two or three days. Some six days after the appearance of the attack I was summoned to see her. There had been no colicky pain for several days, and there remained merely a sensation of "soreness" in the epigastrium and right hypochondrium. Her stomach had been much disturbed by the remedies previously employed, and there was persistent nausea, with fetid breath and foul tongue. Although there had been a febrile reaction, the temperature now did not exceed 100° F. Examination disclosed a readily palpable and large (reaching to the umbilical line) but not hard gall-bladder, very little sensitive to pressure. It was interesting that there had been two similar though much briefer attacks occurring about six months apart some ten years before. The patient could not recall the occurrence of pain from that time until the present. Jaundice was absent in these as in the present attack. Here there was an undoubted acute hydrops of the gall-bladder, with stone probably engaging the cystic duct. The case was under constant observation for two weeks, when, but little diminution in the size of the tumor occurring, I had Dr. Neilson see her, with a view to operation. Consent of the patient was first given, but subsequently withdrawn. At the end of the third week the gall-bladder had diminished to about one-half its original mass, but was still easily palpable. She then was no longer under treatment.

In this case, as remarked, the cystic duct is probably still obstructed by a stone. The infection originating the acute seizure was evidently slight, leaving a simple dropsy of the gall-bladder. If I am right in my surmise concerning the presence of stone in the cystic duct, a cholecystotomy should have been done. This I persistently urged, resultlessly. On inquiry at this writing about her condition, the patient, who had not previously been seen for about a year, informs me that she has remained free from recurrence of colic and regards herself in perfect health; but she states it is not unusual to be conscious of a sensation of weight and discomfort in the region of the gall-bladder. An examination at this writing shows resistance and fulness here; and although, because of a recent increase in abdominal plethora, the gall-bladder cannot be palpated with distinctness, it is evidently still somewhat enlarged. I regard it probable that there are adhesions about it which later will cause trouble.

I have seen many cases similar to the two foregoing, and cite them as specimens of a class.

Two weeks ago a physician brought to me a man whom he presumed to be suffering with recurring attacks of simple gastritis. There were seizures lasting upward of a week or two, in which there were present epigastric pain and vomiting, with intervals of freedom from more than slight pain, but with present gastric irritability for several months. The patient was brought in the interval, and advice desired because of the irritable stomach. As jaundice had never been present, cholecystitis had not been suspected. An examination showed acute sensitiveness in the gall-bladder region and in no other situation. The gall-bladder could not be palpated because of the muscular rigidity

and tenderness. Careful inquiry elicited the fact that the pains were as severe in the right hypochondrium as in the epigastrium. The case was clearly cholecystitis such as demanded surgical interference. The patient was immediately sent to Dr. Deaver, who acquiesced in the necessity for operation, but the patient's consent could not be obtained.

The following strikingly interesting case shows with what few symptoms calculous cholecystitis may develop and continue despite the presence of a chronically very large gall-bladder and stones in the cystic duct:

In May, 1898, I saw, with Dr. Pottberg, a woman, aged seventy years, who complained merely of a dragging sensation in the right side. Dr. Pottberg had noted the presence of a tumor, but was uncertain as to its nature, because of the absence of symptoms. The patient was otherwise in perfect health and without any indications of senility. It was only on close questioning and with difficulty she recalled that several years before she had had at short intervals a few slight attacks of what she regarded as "stomach cramp," for which she had not consulted a physician. Jaundice had never occurred. Examination disclosed a very large and apparently unadherent and but little sensitive tumor, which was plainly the gall-bladder. It caused inconvenience merely by its weight. The diagnosis was chronic obstruction of the cystic duct by stone, with the presence, presumably, of many calculi in the gall-bladder. Immediate operation was advised. This was performed by Drs. T. R. Neilson and H. C. Deaver, at the Episcopal Hospital. Section disclosed a very large and unadherent gall-bladder. It contained over one hundred stones and a great quantity of mucoid material. Two good-sized stones tightly engaged the cystic duct. These were removed and excision of the gall-bladder practised. The patient made a prompt recovery and has been in good health to the present.

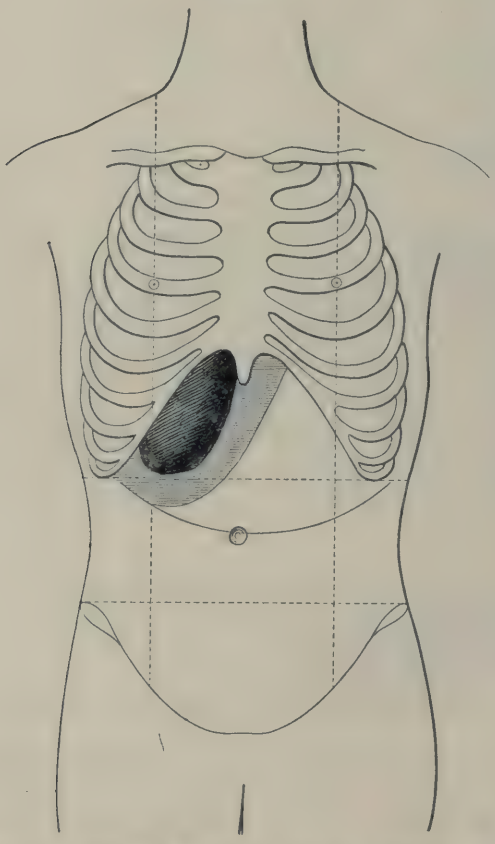
The diagnosis in cases like the foregoing, examples of simple calculous cholecystitis, is readily made if one is on the alert. The history of colicky pain associated with persistent or recurring sensitiveness in the gall-bladder region, even though the gall-bladder be not palpable, should at once lead to a conjecture as to the probable nature of the ailment. A cholecystitis when occurring primarily, apart from a general infection, is very apt to be associated with calculus. Occasionally a case is encountered in which the results of a pericholecystitis, probably following several acute seizures, suggest the notion of latent calculus, although no stone may be present. In such a case adhesions resulting from attachment to the omentum, duodenum, stomach, or colon are the cause of colic or at least of soreness and discomfort in the gall-bladder region. If the gall-bladder should be patent and kinking of its duct intermittently occur, colic may thus arise in the same manner as if a stone were temporarily obstructing the duct. In such cases calculi may have been present, but been voided. I have seen several

cases of this nature. In the following recently observed instance the diagnosis of adhesions was confirmed by operation. The case is a most instructive one.

In this case the presence of attacks of recurring slight colic, often associated with diarrhœa, of persistent sensitiveness in the region of the gall-bladder, of an ill-defined tumor and of interference with the gastric function, caused me to make a diagnosis of chronic cholecystitis with adhesions, probably to the duodenum. It was presumed the condition was dependent upon cholelithiasis.

L. W. T., aged forty-four years, consulted me in December, 1899. For the preceding four years his stomach had troubled him. Briefly

FIG. 1.



Deep shaded area, that of fulness, resistance, and of decided sensitiveness to pressure. Lightly shaded area that of diminished sensitiveness. The whole shaded area, region in which crampy pain is common.

the symptoms were: More or less discomfort at all times in the region of the stomach and right hypochondrium, especially manifest an hour or so after meals. It is more marked when in the erect posture, and is scarcely evident when lying down. No pyrosis; no flatulency. Bowels irregular, with a tendency to looseness, with pains in the gall-bladder region. These pains diffuse over the abdomen, and, following an attack of pain, diarrhœa lasting from a few hours to a day or so

may occur. Twenty years before he had had a liver trouble. Liver was then said to be enlarged; never jaundiced; no lues; no typhoid fever; hue of skin markedly sallow; no icterus; puffy lower lids; acneform eruption on face; area of fulness and sensitiveness in the gall-bladder region and below at the situation of the hepatic flexure of the colon. Situation of tenderness especially that of the gall-bladder region. Decided sensitiveness to deep pressure if extended under the costal margin. Sensitiveness diminished laterally, as is indicated in the shading in Fig. 1. Outline of liver normal. Spleen not palpable. Inferior border of the undistended stomach at umbilicus. Knee-jerks, station, and pupils normal. Several examinations of the stomach contents: Lowered motility; high total acidity, with subnormal HCl; impaired starch digestion. Blood examination: Leucocytes, 7200; red blood corpuscles, 4,350,000; hæmoglobin, 75 per cent. Urine: Specific gravity, 1020; trace of albumin; narrow hyaline casts; glucose absent. Diagnosis: Chronic cholecystitis with adhesions; chronic gastritis. Treatment: Diet regulated; systematic out-of-door (horseback) and breathing exercises. Daily morning stomach douches with hot and cold water, sodium bicarbonate in hot solution, and weak quassia infusion and sodium chloride in the cold. Lavage, succeeded three-quarters of an hour before breakfast by sodium phosphate and sodium sulphate, of each ½ to 1 drachm; sodium bicarbonate and salicylate, of each 10 grains. Nux vomica, nitrohydrochloric acid, and taraxacum before meals. After meals diastase, rhubarb, and ipecac. Priessnitz compress constantly worn; later, flying blisters to the gall-bladder region.

The general condition improved markedly under this treatment, but at the end of two and one-half months, sensitiveness and fulness in the gall-bladder region continuing, I had Dr. Keen operate. The gall-bladder was fixed by adhesions to the duodenum and colon; cystic duct patulous. The gall-bladder free from calculi; its walls thickened. When last seen, six months after the operation, local symptoms had not reappeared and the general health was good.

The case of Dr. Pottberg narrated above is unusual in paucity of symptoms and in freedom from ill effects, the result of the long-existing gall-bladder obstruction. The original infection causing the cystitis, which led to the passage of calculi into the cystic duct, was evidently of feeble intensity and short duration, and a re-infection of the gall-bladder was prevented by complete occlusion of the duct. I shall cite another case of cholecystitis in which the diagnosis was at first somewhat doubtful, the attacks simulating those of angina pectoris. Here there existed bad aortic and mitral disease with imperfect compensation, and chronic nephritis. Although calculous cholecystitis was early suspected, and later demonstrated by the recovery of stones from the passages, an operation which was suggested to the patient six months before it was performed was postponed, because of the risk involved by the bad heart condition. Operation was performed when it was feared that a rupture of the gall-bladder might ensue. This case is related in brief outline only.

Mrs. M. D., aged forty-seven years; first seen in June, 1900. Patient confined to bed. She was then in the midst of a severe anginal seizure. There was substernal and infrasternal pain; marked cyanosis, urgent dyspnœa; very irregular heart, with similarly irregular but high pressure, slow pulse; marked aortic regurgitant murmur and presystolic and systolic (transmitted) mitral murmur. Cardiac enlargement. The liver was much enlarged; the conjunctiva slightly icteroid; albumin and casts in the urine. Apart from the severe pains above mentioned, there were attacks of crampy pain in the centre of the epigastrium, but not then in the hypochondrium. These lasted an hour or two and were associated with diarrhœa. These were not manifest when she was first under observation. The seizures were at first regarded as anginal in character, dependent upon the aortic valve disease, and this notion was borne out by the improvement and marked diminution of attacks under cardiac medicaments. Tumor of the gall-bladder was not apparent until November following, five months after she came under observation in the seizure occurring just before operation, and no marked sensitiveness in the gall-bladder region was at first evident. This had on a number of occasions been searched for, as it was suspected in the early summer that cholelithiasis was a factor in the production of the attacks. The feces were from the first sieved at intervals through the summer and autumn, but no stones were found until November. She was seen in only three attacks, two such as described above, the third in November. In this, associated with the presumed anginal pain, there was pronounced hepatic colic. The gall-bladder was then found much enlarged, and highly sensitive. Jaundice other than icteroid conjunctivæ was absent. Rigors and fever existed with the seizure. I feared an empyema of the gall-bladder and urged the necessity of immediate operation. Operation by Dr. Keen, November 18, 1900. The gall-bladder although much enlarged, contained but fifteen calculi—a few very large and a number quite small. It was distended with a mucoid material and the walls looked as if in a condition of slough. The patient, although very ill after operation, finally recovered. Despite the condition of the heart and kidneys, which render her a permanent invalid, there has been no recurrence of what were first thought to be anginal attacks.

The preceding cases, excluding that of the pericystic adhesions without stone—mentioned to show a later phase of the disease—are common examples of the calculous affection, but such as are not seldom undiagnosed by the general physician. In these cases without obstruction of the common duct jaundice is naturally wanting. Should icterus of minor grade develop—wholly unnecessary to the cholecystitis itself, however, many stones may engage the cystic duct—it is originated by the infectious process invading the common duct or the hepatic ducts and the smaller biliary channels, thus developing a catarrhal cholangitis. It is a matter of common experience in consultation, although the reason for the absence of jaundice is obvious, to be met by the query, if it is a case of gallstone, Why in all this time has not jaundice appeared? So, too, the impression often exists that the occurrence

of very severe pain is an essential factor in the passage of a stone, and of continued suffering with its lodgement. That it commonly is, there is no question, and no greater acute pain in any ailment may be experienced than by the passage of a good-sized calculus through the spiral cystic duct and finally through the papilla of the common duct into the duodenum.[1] It is these cases which are the rule in which jaundice and pain are so prominent that lead to the non-recognition of the exceptions. A stone may be of fair size and be lodged for some time in the common duct, yet from its shape and from the absence of inflammation about it, allow fair passage of bile onward into the bowel, the obstruction, if any, being intermittent; then a slight discoloration of the conjunctivæ only may be present. Usually, however, jaundice of high grade follows in a few days the impaction of a stone in the common duct, which jaundice may lessen and increase as the flow of bile is alternately completely stopped and again partially established, until the stone reaches the termination of the common duct, and finally entirely and more or less permanently occludes it. It is thus usual to find considerable variation in the amount of icterus with obstruction of the common duct by calculus, unlike the case with obstruction from without as by a tumor (carcinomatous growth of the gall-bladder and of the glands of the portal fissure, or of the head of the pancreas). Here, too, another point of importance should be spoken of in the recognition of these cases of calculous obstruction of the common duct, of value in differentiating them from obstructions arising from the presence of a new-growth or pressure by carcinomatous glands. In long-continued obstructions from stone, the gall-bladder commonly, though enlarged originally, finally, by virtue of the chronic inflammatory thickening of its wall, becomes undistensible, shrinks, and is unpalpable; while in obstruction of the duct from pressure by a growth a gall-bladder tumor is usual.[2] This, which has been termed the law of Courvoisier, although it must not be depended upon invariably, is of value in diagnosis, as is shown in the following case. This case, in which the diagnosis was confirmed by operation, also illustrates one of the vagaries of cholelithiasis. It is one in which, with obstruction of the common duct by a massive, tightly adherent calculus, little preceding history of colic could be obtained. The stone was finally borne without pain, and jaundice and debility almost alone, after a few weeks of colic, indicated to the patient the presence of her illness.

Miss D. B., aged fifty-two years; referred to me by Dr. A. G. Bennett, of Mahaffey, Pa. The patient stated that she had had more or

[1] I recall that the late George Harley taught that pain invariably accompanied chronic obstruction of the common duct by stone.

[2] But if the gall-bladder contain many calculi, or its duct is early occluded with presence of fluid from simple dropsy or empyema, this rule will not hold.

less "stomach disorder" for ten years, but her general health had been little affected thereby. The symptoms consisted chiefly of slight attacks of what she regarded as epigastric pain, lasting about a half hour and then disappearing. There would be intervals of three or four months between these spells. These slight attacks of presumed "stomach colic" thus occurred for about ten years. They were unassociated with any special gastric symptoms or with noticeable jaundice, until lately. The patient was first seen June 12, 1901. In November preceding she had epigastric soreness, with some little crampy pains in the right hypochondrium. In December there was some colic, lasting about three days, with more or less continuous slight pain, referred to the epigastrium, for two or three weeks. Pain and even soreness then disappeared, and remained absent for a week or two, following which jaundice suddenly appeared when entirely free from pain, and continued for about three weeks. With disappearance of jaundice colicky epigastric pain again recurred, but no cramp was recalled to have been present in the right hypochondrium until she was once more jaundiced, about a month before I saw her. After the first attack of jaundice the skin cleared fairly well, but the scleræ remained icteroid. Since the recent attack she has been quite persistently very deeply jaundiced, but is without pain. The only symptom of that nature is that when lying on the left side discomfort in the epigastrium is experienced. Her weight a year ago was 175 pounds; present weight, 130 pounds. The greater part of the 45 pounds had been lost since the first attack of jaundice. There are no especial dyspeptic symptoms. There are present complete anorexia, extreme mental torpor and physical debility, pruritus, and obstinate constipation. The stools are of pipe-clay hue; the urine is concentrated and of porter color. Although the skin is of a deep saffron hue, she states the jaundice tint had been more marked a week or so before.

Physical Examination. Abdominal walls flaccid; with full inspiration inferior border of the right and left lobe of the liver is readily palpated. Edges sharp, firm, and even; liver somewhat enlarged; gall-bladder not palpable, certainly not enlarged, for the fingers could be depressed below the liver's edge. No sensitiveness to manipulation in the gall-bladder region, and none elsewhere save just below and to the right of the ensiform cartilage, but even here not marked. Spleen not enlarged. First heart sound enfeebled.

Blood. Several examinations (Dr. Ghriskey) average: Leucocytes, 8500; red blood corpuscles, 4,200,000; hæmoglobin, 77 per cent. Several examinations of the stomach contents: Total anacidity; the removed contents always presented the ordinary water-soaked appearance common in cases of achylia; small amount of gastric mucus. No lab reaction with milk incubated twenty-four hours. Gastric motility unimpaired.

Urine. The urine is deep golden-brown; heavily bile-stained, opaque, acid, specific gravity, 1030; well-marked albumin reaction; epithelial, granular, and hyaline casts and red blood corpuscles present.

Diagnosis. Obstructive jaundice, with stone in the common duct; past calculous cholecystitis; nephritis, the result of the chronic cholæmia; probably hepatic cirrhosis in process, due to obstruction. Patient informed of the diagnosis and operation advised. Medical treatment for removal of stone was regarded as futile to attempt.

Patient admitted to my service at the Episcopal Hospital. The attending surgeon then on duty, Dr. T. R. Neilson, saw her with me and concurred in diagnosis. Carcinoma of the gall-bladder and gall ducts was, of course, considered, but was excluded.

To diminish risk of hemorrhage on account of the high grade of jaundice, with the approval of Dr. Neilson I instituted the following preparatory treatment, which was continued for two weeks. It is such as in the case of small, unencysted calculi is sometimes of service in causing their expulsion: Daily morning stomach douching with alternate hot (sodium bicarbonate) and cold (sodium chloride) solution; one-half to one hour before each meal there was administered a combination of sodium sulphate, phosphate, and bicarbonate, in hot water, with the addition of tincture of nux vomica; diet carefully regulated; extract of pancreas as a digestant. Two daily high enemas of normal salt solution—the one hot, the other cold—were given. Under the above treatment the amount of urine, previously so scanty, increased to upward of three quarts daily. Bile appeared in the stools, but the hue of the skin was little if at all changed.

Three days prior to operation I ordered calcium chloride by enema in place of sodium chloride.

Section by Dr. Neilson, June 27th: Liver somewhat enlarged; surface firm; gall-bladder shrunken and empty. A large stone was found densely adherent in the middle portion of the common duct. It was removed with great difficulty. Its size and shape is that of a large-sized olive. It was of enormous size to have so far engaged the duct. The probability is that its accretion occurred *in situ*, where it must have been for a long period. Considering the dense adhesions about it and its bulk, it is impossible to conjecture the manner in which under the preparatory treatment instituted bile should have escaped passed it; but that such was the case was shown by the appearance of the latter in the feces, as stated.

The patient made a good recovery, and subsequently underwent treatment for removal of the conditions engendered by the cholelithiasis. Mention of this treatment is made in the latter part of the paper.

I have here brought together a small group of interesting cases recently encountered which illustrate certain phases of gallstone diseases. These cases represent simple catarrhal cholecystitis, without obstruction; with obstruction; with dropsy of the gall-bladder; with indications of beginning empyema; of pericholecystitis with adhesions the result of past cholecystitis, probably calculous; of chronic obstruction of the common duct by stone, with the usual accompanying jaundice and shrunken gall-bladder.

I shall briefly consider the recognition of such cases as these, the occurrence of which is common. Frank, outspoken cases of cholelithiasis, with severe colic, jaundice, and passage of stone, are so easily recognized that they need neither illustration nor remark. It is the frequent cases without discovered passage of stone and without jaundice that are apt to mislead. The points of greatest importance in the detection of these is to have the fact of their common occurrence in

mind; to recall that however transient the duration of the self-diagnosed "stomach pain," if it is recurring the possibility of its being of gallstone origin is worth considering; to be not satisfied with the statement of the patient that the seat of pain is the epigastrium, but to have him carefully note in the attacks if it has not origin and greater intensity to the right, and if possible to examine the patient during or immediately after a seizure; then careful palpation will usually establish the diagnosis. In the recognition of cholelithiasis, among a variety of simulating conditions it is necessary to exclude simple gastralgia; gastralgia the result of adhesions, as, for instance, from past ulcer; the gastralgia of gastric and of duodenal ulcer; that of adumbilical hernia (in my experience, a not unusual source of presumed simple gastralgia). Ileus and acute pancreatitis must also be borne in mind.

Space is not here at hand for systematic discussion of differential diagnosis. I shall merely refer here to a few distinctive points which I have found of especial value.[1]

The pain of latent duodenal ulcer is apt to confuse; but it, like the pain or gastralgic seizures of gastric ulcer, commonly bears more or less definite relation to the ingestion of food, occurring immediately, or, often with definite regularity, two or three hours after eating. Other usual symptoms, among which is the locality of the pain, assist in its differentiation. Adumbilical hernia, the pain of which, as before remarked, is often mistaken for pure gastralgia and even for gastric ulcer, has its seat of intensity and sensitiveness at the site of the gripped point of omentum, the small nodule of which is commonly easily felt with careful palpation in the median line above the umbilicus. Perigastric adhesions often cause obstinate gastralgia, but they are not apt to simulate the pain of calculus except when the pylorus or duodenum is adherent to the gall-bladder, and then there is or has been usually a calculous cholecystitis. Similar gall-bladder adhesions to the duodenum, omentum, or colon causing intermittent obstruction of the bowels, with alternate diarrhœa and constipation, of which I have seen several instances, are often puzzling to diagnose. Careful interrogation as to past history of liver colic and the presence of a sensitive gall-bladder region assist materially in their recognition.

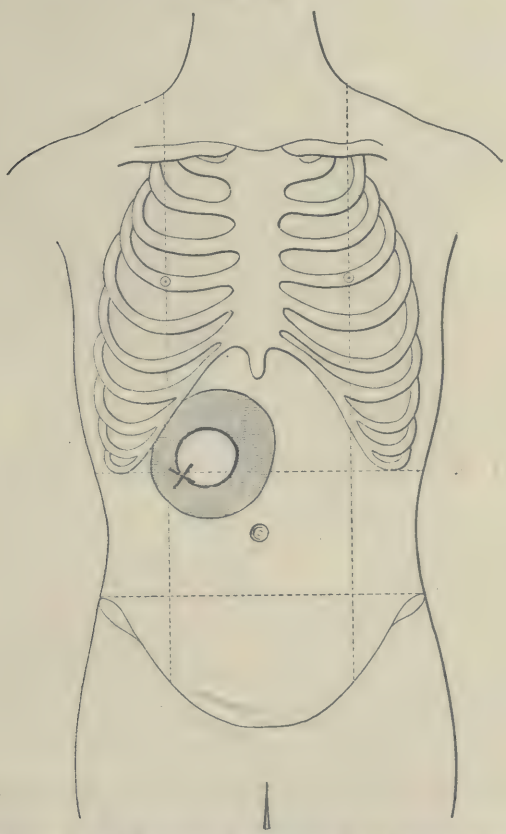
Spasm of the pylorus occurring with gastrosuccorrhœa and the pains of periodic gastrosuccorrhœa, occurring as these pains are most apt to, through the night, has misled. An interesting case of this sort I recently reported to the American Gastro-enterological Association, but it is not yet published. It is worthy of brief outline here. The

[1] I have not discussed the use of the X-ray in the diagnosis of cholelithiasis, since in the class of cases in which its assistance would be of real value—stone in the cystic duct or in the common bile duct—it cannot at present be employed to obtain results.

patient was under treatment with several practitioners for supposed gallstones for a year and a half before being sent to me by the late Dr. Charles Wirgman.

T. B., aged thirty years; store porter, of spare build; weight about 120 pounds; no typhoid; no syphilis. He had been the subject of attacks of sharp, cramp-like pain in the abdomen for several years. The first attack occurred three years before; then there was a lapse of one and one-half years; the seizures were very frequent in the past year and a half. Pains suddenly develop, without previous warning, in the epigastrium and to the right, in the pyloric region, shooting thence

FIG. 2.



Inner circle area of fulness and firmness very perceptible when stomach inflated with air; then this area too tympanitic. The cross indicates the starting point of cramp, during the occurrence of which a prominence approximately as denoted by the shaded area appears. Pains radiate thence over the abdomen and through the right hypochondrium to the back.

toward the epigastrium, umbilicus, and into the back; pains may last one or two days, but commonly their duration is but a few hours. Never jaundiced. Attacks occur, as a rule, between 1 and 3 A.M. Nausea is apt to accompany colic, but never vomiting unless self-induced; the vomit is then copious in amount (he states one to three quarts of acid fluid). Pain relieved by free emesis. Eats a cold lunch at noon and a hot supper, when very fatigued, at 6 P.M., retiring at 10 P.M. Twenty pounds loss in three years. He believes his previous occupation, that of a car driver, necessitating exposure and hasty, irregular eating, responsible for his ailment.

Physical Examination. Mitral presystolic murmur; heart unenlarged; much dilated stomach; no tumor or sensitiveness save in pyloric (or gall-bladder) region, and then only during presence of pain. Gastric capacity, 3400 c.c. (after having been accustomed to the use of the tube); pronounced stagnation of food; sharp hyperchlorhydria. Inflation showed fulness and firmness in pyloric region —on inflation, prominence the size of a hen's egg, tympanitic on percussion and not very sensitive—a cramped pylorus. Patient seen in several seizures. Situation of pain rather suggestive of gallstone colic. Fulness and firmness in region of pylorus, a little below and to the left of normal situation of the gall-bladder. (Fig. 2.) Here there appears the above-mentioned palpable prominence, behavior of which to manipulation is unlike that of the gall-bladder. Tube introduced during seizure invariably removed a large quantity of fluid, 1 to 2 litres, which presents the appearance of gastric secretion; very little food particles evident if some hours after a meal; high percentage of HCl present; immediate lavage with sodium bicarbonate solution instantly terminates attacks. This was the case in the first seizure in which I saw him, and has been invariable since. The employment of the tube taught the patient, and thus he always was able to abort an attack.

Attacks ceased in a few months on local treatment with silver, alumnol, and bismuth, and daily lavage. The patient was under constant observation for three years, and then seen at intervals to the present. The local treatment was continued for several months and then an interlapse, to be re-begun with recurrence of seizures. At the end of about a year they ceased finally, and none have now been present for several years. At first the advisability of an operation on the pylorus or a gastro-enterostomy was considered and arranged for, but the patient would not finally consent, as his impoverished condition would not permit him to neglect his work, a family being dependent upon him for support.

This case is evidently one of past latent ulcer, followed by cicatricial contraction of the pylorus, with subsequent dilatation of the stomach. The attacks were those of gastrosuccorrhœa, with sharp pyloric spasm. The correct diagnosis was only possible by the employment of the stomach tube. As remarked, two practitioners of note prior to his consulting Dr. Wirgman had had the case under observation for one and a half years, regarding it as one of gallstone disease. No gastric examination had been made, and he had never been seen during an attack. Gallstones had been unavailingly searched for. Cases of this sort are not common, but are readily enough recognized if one is on the alert and employs modern methods of examination.

Simple gastralgia, the result of pure hyperchlorhydria, is a common enough affection, and may for a time be quite difficult to separate from mild catarrhal calculous cholecystitis. The pain, however, bears a more definite relation to food than does gallstone colic, occurring pretty definitely two to three hours after meals, but may, as in gallstone colic and in periodic gastrosuccorrhœa (which has gastralgia as an accom-

paniment), be most usual at night, although no hypersecretion accompanies the gastralgia. Commonly treatment instituted for the hyperchlorhydria promptly establishes the diagnosis. An illustrative case is the following:

J. M. S., aged sixty-two years; was first seen June 2, 1902. Referred by Dr. Walter Freeman. For the past one and a half years, following an attack of supposed grip, gastralgic pain, occurring at intervals of from four to five months up to last March. Since March occurring every day or so; past few weeks rarely misses a day; occurs especially when he applies himself at desk work. Six to eight years ago he had similar attacks for a short time. These disappeared entirely when he lived more in the open air. Occupation now very sedentary; takes no exercise. Appetite good when free from pain; constipation. Pain appears in the centre of the epigastrium and passes through both hypochondria to back; lasts one to three hours; diminishes in severity when he lies down; hot applications relieve. No "heartburn," occasionally water-brash; pain not especially influenced by food, but eating may relieve. No typhoid fever; no lues.

Physical Examination. Nothing noteworthy; heart normal; no sensitiveness in gall-bladder region in several examinations, or in other portions of the abdomen; stomach normally placed and undilated. Knee-jerk, station, and pupils normal.

Several examinations of the stomach contents: Hyperchlorhydria; marked atony. Urine: Trace of albumin; glucose absent; a few hyaline and granular casts; free uric acid; numerous red blood corpuscles, probably originated through irritation by the uric acid precipitated in the tubules.

Cessation of attacks was very prompt in this case under regulated diet; Carlsbad salts on rising; a full dose of an antacid three hours after meals and a combination of nux vomica, cannabis indica, and codeine before meals—codeine was taken for a short time only. At the end of a month nothing save a sodium sulphate laxative in the morning and an antacid three hours after meals were prescribed. No pain has occurred to the present (March) from two weeks after he was first seen, now nine months ago.

A similar but much more obstinate case of presumed pure gastralgia now under treatment is also of diagnostic interest. I had first suspected there might be latent cholecystitis, and examined him many times resultlessly for presence of sensitiveness in the gall-bladder region.

C. J. B., aged sixty-one years; first seen September 9, 1902. In good health up to two and one-half years ago, when epigastric pain developed. Pain occurs two to four hours after meals, and is most common at night, then there may be a much longer lapse. He fancied eating did not allay the pain, but after he had been under treatment assured me that eating is invariably remedial, pain occurring soon ceasing after a glass of milk and a few crackers. Pain in centre of the epigastrium. Seat of greatest intensity immediately below the ensiform; thence radiates, when severe, through to the back. Later, he stated, the seizures have been very severe, pain sharp and paroxysmal, but at times merely a dull ache. Duration an hour or two. No nausea

or vomiting; appetite good, but fears to eat. For some months has been on starvation diet, and is debilitated in consequence. Constipation, but regularity maintained by laxatives. Best weight, 215 pounds; now, 190 pounds. Moderate drinker in the past, now for years a total abstainer; moderate tobacco user; no syphilis. Some years ago malarial fever; no other ailments; father died of liver disease; mother, aged fifty-five years, of cancer of the stomach. He feared the latter ailment, and was much depressed mentally.

Physical Examination. Knee-jerks, station, and pupils normal; stomach normally placed; no point of sensitiveness anywhere about the abdomen; gall-bladder region in many examinations totally free from sensitiveness; heart normal. Several examinations of the stomach contents: Sharp hyperchlorhydria; motility normal; three hours after a meal of steak, bread, and water, total acidity 124. HCl equal 0.365 per cent. Urine: Fair trace of albumin; hyaline casts. The patient was seen in one attack. Hypersecretion and hyperchlorhydria were found to exist. Lavage with warm sodium bicarbonate solution quickly dissipated the pain. Examination during and subsequent to the attack revealed no gall-bladder sensitiveness.

Treatment. A morning laxative of equal parts of sodium sulphate and phosphate. Before meals, cannabis indica, codeine phosphate, hyoscine hydrobromate; a full dose of antacid three hours after meals. Ordered to eat between meals when possible, then no antacid. After a week's treatment pain occurred rarely by day, but was more usual three or four hours after the evening meal, and from 1 to 2 A.M. It had lost its intensity markedly—now a dull ache, when formerly it was often an unbearably severe colic. For the first two or three days pain not markedly influenced by antacids, but subsequently and now invariably checked within a few minutes by a teaspoonful of a powder containing equal parts of sodium bicarbonate, magnesium carbonate, and oleosaccharate of peppermint. Codeine discontinued at the end of a week, and strontium bromide, cannabis indica, and hyoscine substituted for the above combination. This was again replaced in ten days by silver nitrate and hyoscyamus. Pain having entirely ceased under this and the antacid, which he now took regularly three hours after meals, all medicine save the antacid was discontinued. No pain occurred for two weeks, when a night indulgence in ice-cream, cakes, and lemonade provoked a transient recurrence. He now takes the antacid regularly, and the stomach is douched with silver nitrate solution twice a week. Dull pain now occurs rarely at night, quickly dissipated by the antacid. I regard this case as one of pure gastralgia. There are no indications of adhesions. The possibility of latent gastric ulcer is considered. Gallstone colic is positively excluded.[1]

Although acute pancreatitis, with or without disseminated fat necrosis, is an affection of comparative infrequency, its association with gallstone disease, in consequence of the latter, is well known. Acute and chronic pancreatitis may be originated through the presence

[1] Since the above writing (three months) the patient has been free from attacks. The later treatment, which has been most beneficial, is courses of alumnol and silver used through the stomach tube.

of a calculus in that portion of the common bile duct near its duodenal orifice, at which point pressure may be also exerted on the contiguous pancreatic duct, interfering with the flow of pancreatic secretion into the bowel or admitting of the retrojection of bile into the pancreatic duct, as suggested by Halsted and Opie. If, as is the case in about one-third of human subjects, there is either merely the single pancreatic duct of Wirsung, or no communication between the latter the subject of occlusion, and that of the accessory pancreatic duct (of Santorini) which opens into the duodenum separably from the duct of Wirsung, conditions favorable for widespread fat necrosis and pancreatic disease exist. The pancreatitis in such cases is the result of long-continued obstruction plus infection. The obstruction offers conditions favorable for the growth of micro-organisms which have passed from the duodenum into the pancreatic duct and thus into the vulnerable organ. Without such infection it is probable that, by obstruction alone, a chronic interstitial pancreatitis may originate by virtue of the irritation resulting from the long-continued damming up of the pancreatic secretion.[1]

Without cholelithiasis, and without such obstruction of the pancreatic duct, it is likely that infection of the pancreas from the duodenum, causing acute or chronic inflammation, may occasionally occur. Such a condition may be especially looked for in cases of chronic gastritis of bacterial origin. In several cases of chronic gastritis which I have had under observation in which inflammatory changes in the secretory glands exist, presumably the result of infection, there were indications of chronic interstitial pancreatitis which I regarded as due to a similar transmitted infectious process.

The following most instructive case is in all probability one in which acute pancreatitis was so produced. It is of extreme interest, since the diagnosis by the attendants, who had been misled by the previous history, was at first that of collapse from perforation the result of a gallstone, and finally that of impaction by a biliary calculus without perforation. This case forcibly illustrates the difficulty sometimes encountered in differentiating between acute pancreatitis and gallstone disease. Briefly the points are: There had been two attacks of acute gastritis, in which I saw him; following which gastralgia appeared. There was a chronic subacid gastritis (with erosions), probably from mouth infection. About two years after the second attack of acute gastritis, while in another city, there suddenly developed overwhelmingly severe pain in the abdomen, followed by collapse. The diagnosis of his numerous attendants was as stated above. Section demonstrated

[1] See a paper by Opie, The Relation of Cholelithiasis to Disease of the Pancreas and to Fat Necrosis, THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, January, 1901.

entire absence of cholelithiasis or any of its consequences, and the presence of some old adhesions and of recent lesions such as are indicative of acute pancreatitis. The case is as follows:

C. M. L., aged forty-seven years; plethoric habit; weight, 210 pounds; sedentary occupation; very little exercise or fresh air; indiscreet in diet; moderate alcoholic indulgence; tobacco in excess; no lues. Attack of acute gastritis in the early part of 1897, in which I attended him in consultation with the late Dr. J. M. Da Costa. A similar attack a year later, in which I also saw him. On each occasion the symptoms were those of a general infection, with a local expression in the stomach. Vomiting had occurred at the early part of the attack; stomach-contents foul smelling; free HCl and the ferments absent; excess of organic acid; fever; epigastric sensitiveness and pain; congestion of the base of the right lung in each seizure. Urine contained albumin, hyaline and a few granular and epithelial casts. Following the first seizure of this sort there were recurring spells of mild gastralgia, in duration an hour or two and occasionally longer. Pain rarely severe, and commonly easily checked by lavage and the use of codeine. Repeated physical examinations gave no indication of the pain being other than gastralgic. Several examinations of the stomach-contents in the interval during two years always showed: Invariably absence of free HCl; pepsin and lab ferments absent; the pre-enzymes in traces only; acidity low (10 to 20). Blood-stained bits of the mucosa occasionally found in the wash water, presenting the usual appearance of erosions. Gastric motility normal save during the acute seizures. Stomach undilated and normally placed. The urine in the interval of attacks of acute gastritis was practically normal. There existed a severe type of pyorrhœa alveolaris. This had been present for years, and had never received adequate attention. Bacterial cultures from the gingival margins showed among many other organisms the staphylococcus pyogenes albus and aureus.

Diagnosis. Attacks of acute gastritis intercurrent with chronic glandular gastritis; gastric erosions; gastralgia; the gastritis probably the result of the alveolar pyorrhœa. The gastralgia was regarded as probably of nervous origin, although the possibility of its arising from perigastric adhesions the result of long-continued gastritis was noted. Gastralgic pain tended to recur despite medical treatment, and after the second attack of acute gastritis the patient was persuaded to stop work and take a six weeks' summer holiday. Gastralgic pain had then been annoying him considerably. This immediately and entirely ceased from the day he abandoned business. He went into camp in Canada; tramped, fished, and shot, eating ordinary camp food and frequently getting wet. This exposure, with rough food and a great deal of active exercise, in the nature of things should have been productive of attacks of gastralgia had they been due to adhesions. Their non-recurrence and their complete absence for some months after his return, despite active tennis, suggested these pains were of nervous origin. The following winter (1898–99), despite close application to business and general unhygienic living, he was in better health than he had been for a long time. The succeeding summer his outing was brief and his application to work close. In the autumn following (1899) I saw him in two attacks of presumed gastralgia; in one he was confined to bed for

twelve hours, and the pain was quickly relieved by lavage. There had been diffuse gastric colic, associated with stagnation of food and decomposition of the ingesta. The cardia was in spasm, so that the stomach tube was entered and withdrawn with difficulty. The second attack immediately followed a dinner party. The pain had been of a half-hour's duration when I saw him in my office, and was instantly checked by lavage.

Some months later, while in another city, he had an attack altogether unlike any of the preceding. There suddenly appeared severe abdominal pain and vomiting. On the arrival of his physician he was in a state of collapse. There was stated by his attendant to be "cyanosis, shallow thoracic breathing, diffuse abdominal pain and tenderness" (the pain and tenderness thought by the attendant to be largely epigastric and hepatic), "a rapid, thready pulse and cold sweat." Calculous cholecystitis, with rupture of the gall-bladder, perforating duodenal or gastric ulcer, it was reported were thought of, but the condition was so alarming that little examination was immediately possible to determine the exact diagnosis. It was with difficulty that he was rescued from the collapse which had so suddenly occurred. For three days following it was reported that he was so ill that he was unconscious of his surroundings. There were fever (101° to 102½° F.) and incessant hiccough for about a week. There were "congestion of the base of one of the lungs" and "albuminuria and a slight biliuria." In addition to his regular attendants he had been seen by several medical consultants of eminence and a surgeon of equal note, and it was unanimously agreed that the case was undoubtedly gallstone, with possible perforation, and if not this, at least impaction of a large stone in the duct. Operation was regarded as essential, but his condition did not warrant it being undertaken until about three weeks after the onset of the seizure. The diagnosis of either perforation by a gallstone or of impacted calculus was arrived at by the attendants through a process of exclusion, and because the previous history had made it certain to their minds that the various gastralgic attacks and those of acute gastritis which had occurred in the past were undoubtedly only expressions of the vagaries of cholelithiasis. Upon this there was apparently no dissension, although in correspondence with the attending physician I urged that there had been nothing in the nature of the previous seizures to suggest this; that gallstone colic had then been carefully excluded.

Section disclosed the following: Patient's abdomen very thick walled; adipose tissue at least three and one-half inches; gall-bladder and bile ducts normal; no present or past indications of gallstones. Instead there existed evidences of recent peritonitis; a mass of adhesions binding the hepatic colon, stomach, and pancreas, some recent and some old. Omentum thickened. Pancreas adherent to stomach; *inflammatory mass about and involving an enlarged pancreas.* The operation had to be conducted with great celerity because of the patient's condition, and, it was stated, little time was permitted for examination after separation of adhesions. It was, however, noted that the pancreas was much enlarged, and this enlargement at the time was thought to be the result of a malignant growth. The subsequent history of the case has disproved this. The patient is now living and in good health. As I remarked, I have no doubt that the attack was

one of acute hemorrhagic pancreatitis—an acute pancreatitis of infectious origin perhaps engrafted upon a chronic inflammatory condition of this organ. The infection originating the pancreatitis probably bore some relation to the long-existing chronic glandular gastritis, which itself was presumably due to the continued passing of pus organisms from the mouth into the vulnerable stomach.

The origin of the old adhesions about the stomach is in doubt. The two attacks of gastritis spoken of were unaccompanied by indications of perigastritis—at least the local inflammatory conditions were not then regarded as sufficiently severe to suggest this. Subsequent to operation the patient recalled that years before he had had a fall, striking the abdomen, and it was thought possible that adhesions might have so arisen. That these old adhesions about the stomach bore some relation to the earlier attacks of gastralgia I have no doubt, but that they were the sole cause of this I question, for the reasons cited.

This case well illustrates the difficulty that may attend the separation of an attack of acute pancreatitis from presumed perforation by a gallstone, and indicates how a previous history of epigastric pain may mislead even the most skilled diagnostician. But for such a history, which at once led to the diagnosis of gallstone disease by his attendants, in consequence of which the question of pancreatitis was not, I believe, even considered, it might have received attention. The sudden onset, when in presumed good health; severe abdominal pain; vomiting of at first the contents of the stomach and, later, copiously of bile; the rapid appearance of collapse, continuing, with the occurrence of obstinate hiccough and the like, as detailed, were very suggestive.

The Treatment of Cholelithiasis. There is no solvent for gallstones in the gall-bladder or in the bile passages. The employment of sodium cholate, of sodium succinate, and sodium oleate; of the more rational sodium salts presumed to have some cholagogue effect, such as the phosphate and sulphate; of the old French mixture of ether and turpentine, and of chloroform, is no longer favored by the intelligent physician with the expectation of dissolving calculi in gall-bladder or bile ducts. I confess that some fifteen years or more ago I was an adherent to the contrary notion, and, as a disciple of George Harley, for several years religiously saturated my gallstone cases with sodium cholate and the like, with vain expectation of promoting solution and expulsion of calculi. After a few years of increasing familiarity with the pathology of cholelithiasis, aided by the teaching of the operating and post-mortem table, I became convinced of the futility of the solvent treatment. Treatment of active cholelithiasis is now justly very largely abandoned to the surgeon. There is no medical treatment for persisting dropsy of the gall-bladder, or for obstruction of the cystic duct; for seropurulent or purulent inflammation of the gall-bladder, or for stone long lodged in the common bile duct. But it is unnecessary, and the surgeon is usually unwilling to accept that we shift to him the cases

of simple calculous cholecystitis, presumably without obstruction—cases such as those first cited—until after a fair effort to dissipate the ailment without the knife. If the patient is in a position to have the best done for him at home, and, if necessary, to visit Carlsbad for a season or more, even though the attacks at first show a tendency to fairly persistently return, should they remain mild in character and should enlargement of the gall-bladder not be evident on repeated examination, nor persistent sensitiveness be present, it is proper that such cases be not hurried to the surgeon. Medical treatment, however, is not to be instituted with the view to the solution or extrusion of calculi, but with the object of both controlling the inflammatory catarrhal process in the gall-bladder and of preventing its recurrence, trusting with its abatement that the calculi present will no longer create trouble. It seems probable, as before remarked, that gallstones do not mechanically develop cholecystitis, whereby their presence is manifest. Our present knowledge of the pathology of that affection is against this old notion. It is also likely that only very rarely does attempted expulsion of a stone from the gall-bladder occur without a coincident cholecystitis, the latter, as Kehr remarks, being actually the force that initiates the movement of the stone. Cholecystitis is a very frequent condition, and is far more frequently latent than active, for with presumably almost 10 per cent. of adults carrying these concretions, but possibly somewhat more than 5 per cent. of this very large number have recognizable indications of their presence.

Briefly, I should place the necessity for surgical interference in these cases of catarrhal cholangitis, without presumed obstruction of the duct, in this wise: If the patient is well-to-do, and can spend a season or two at Carlsbad; if there is no strong family history of cancer;[1] if the cholecystitis is recent and of mild type and shows a tendency to no persistent recurrence after some months of treatment, surgical intervention, although not improper, may be regarded as yet unnecessary. Should there be an old history of recurring pains, and the attack for which one is consulted suggests cholecystitis, I regard the case as immediately surgical, for in such a one further recurrences are probable, and the likelihood of pericystic adhesions is strong. Concerning the question of necessity for surgical intervention in cases of stone in the common duct, my view is that these should be operated on no later than a month after a jaundice has developed; since with prolonged obstruction, and with so few if any adequate means at hand to promote passage of the stone, and with danger of complication so vital, it is

[1] The development of carcinoma of the gall-bladder is favored by the presence of gallstones; about 14 per cent. of gallstone subjects develop cancer of the gall-bladder (Kehr). Courvoisier found gallstones present in 87 per cent. of cases of carcinoma of the gall-bladder, and Ames in 95.4 per cent. (quoted by Kehr).

unmedical and unscientific to delay. A stone sufficiently large to completely obstruct the duct, after a month's impaction, in the vast number of cases, is lodged permanently unless removed. No amount of oil or Carlsbad treatment here after this lapse is likely to be efficient. Although jaundice may be temporarily diminished, the stay of the stone will be uninfluenced, while, in consequence of the persistent back-pressure, pathological alterations in the liver structure are soon in progress. Hepatic cirrhosis is a not uncommon result of long-continued biliary obstruction, as are, under the influence of the cholæmia, changes in the kidney. In the case of Miss D. B. related, although the stone had probably not been carried many months, the liver already displayed indications of cirrhosis, and a pronounced nephritis was present, of presumed cholæmic source. This case well illustrated the utter futility of medical treatment in a subject with stone of large size fairly long lodged—the inutility of any drug, however active, as a stone solvent or as an aid to stone expulsion. In this case accretion of the stone probably had occurred in the common bile duct, since it may be regarded as too massive to have passed the cystic duct without more marked symptoms than were originally present.

Other and not remote dangers of prolonged obstruction of the duct to be mentioned are perforation of the duct and pancreatic disease—pancreatic fat necrosis, and acute or chronic pancreatitis. Pancreatitis may follow very shortly after the lodgement of a stone in a situation to obstruct the duct of Wirsung. Cases are reported in which, as stated by Opie,[1] decided pancreatic lesions have followed forty-eight hours after the onset of symptoms of impaction of the calculus, a period too short even for the production of marked jaundice. Although such cases are unusual, the later occurrence of pancreatitis in consequence of obstruction is less so, and is, with other risks, one which physicians must consider, not too long delaying surgical co-operation.

The one object in the treatment of simple cholecystitis is to endeavor to render quiescent the inflammatory process in the gall-bladder and prevent, rather than favor, the passage of a calculus from that viscus. During and following the acute seizure active purgation must be avoided, as must the use of all measures which are presumed to have cholagogue effect. Under no circumstances, even in the quiescent period, must massage of the gall-bladder or of the gall-bladder region be attempted with the idea of diminishing the size of this organ or of assisting to expel its contents. Should a gall-bladder be palpable after an attack, its duct is in all probability obstructed, and the only treatment is surgical. The risk of rupture of an inflamed gall-bladder through massage is not slight. Morphine must be employed with cau-

[1] The American Journal of the Medical Sciences, January, 1901.

tion in acute cholecystitis because of the danger of masking the local inflammatory condition, and because of the effect the drug may have upon the stomach, acting, as it so frequently does, to later enhance the already existing gastric irritability. Nausea and vomiting and pain, save when a stone is presumably already in passage, should be controlled by other means. *Persistent* nausea and vomiting in simple acute cholecystitis probably indicate that the calculus has already entered the cystic or common bile duct, and even if such is not the case, vomiting reflexly favors the engagement of a calculus.

In the treatment of a case of cholecystitis in the interval it is important to ascertain the condition of the motor and secretory gastric functions, and to appropriately treat any existing abnormality. Chronic gastritis frequently accompanies cholelithiasis, and when the former is of mycotic origin it favors the occurrence of the latter. The hygiene of the mouth should likewise receive attention, that infection of the stomach from diseased teeth or gums be obviated. It is held that gallstone suspects, irrespective of the condition of the motor or secretory gastric functions, should take food at short intervals, with the idea that stasis of bile in the gall-bladder and resulting colics be thus rendered less likely. Clemm, of Darmstadt,[1] for instance, while stating that all catarrhal gastro-intestinal affections should be thoroughly treated, suggests that "there should not be more than two or two-and-one-half-hour intervals between meals, with milk between at least twice," and that "a glass or two of milk should be taken before rising in case of the slightest suspicion of stoppage of the flow of bile," and that "the earliest and last meal should be principally albumin and fats;" and Kehr, who is also an advocate of frequent feeding, urges that a meal be taken on retiring. While it is true that during fasting the gall-bladder acts as a reservoir for bile, and that frequent feeding favors its direct flow into the bowel, the risk of increase in gastric atony, should this exist, and of aggravation of the gastro-intestinal catarrh so often present, with transmission of this catarrhal process from the duodenum to the bile duct, is sufficiently great to necessitate caution in the matter of very frequent meals. Feeding in this way is only indicated in those with well-preserved gastric motility or with hypermotility, and especially in such cases with hyperchlorhydria. The interval of meals should thus depend altogether upon the ability of the stomach to empty itself and largely upon the condition of the secretory function. In cholecystitis, as there is no interference with the passage of bile and pancreatic juice into the intestine, and as the gastric secretory power may be normal, no very special diet is essential.

[1] Wiener med. Presse. Quoted in the Journal of the American Medical Association, September 6, 1902.

The food must, of course, be plain and easy of digestion; high seasoning must be avoided and rich entrées and pastry tabooed. No digestant is indicated if the gastric secretory power is normal and proper insalivation of food is enjoined. In obstruction of the common duct, in which there may be coincident obstruction of the pancreatic duct, as with the stone in the diverticulum of Vater, the diet should be largely albuminous, and food into which the composition of starch enters little if at all allowed. If substances containing starch are eaten, the starch should be either first dextrinized or diastase should be administered. Pancreatic extract can be of little real value as a digestant if the gastric secretory function is normal or heightened, as destruction of its ferments in the stomach is certain; but with subacidity or anacidity, fairly frequently present in these cases, pancreatic extract may be freely given with meals to serve the triple purpose of an albumin, starch, and fat digestant. It is then probably of more value, by virtue of its contained steapsin, than is the conjoint use of papain and diastase alone, which later are practically without action on fats.

Gastric atony accompanying cholelithiasis is best treated by daily morning stomach douching with alternate hot and cold water; weak sodium bicarbonate or Carlsbad salt solution in the hot water and sodium chloride in the cold—the last is preferably a weak quassia or calumba infusion. In all cases there is prescribed sodium sulphate either alone or in one of the Carlsbad combinations, such as the Carlsbad salt in powder or in crystal form,[1] or Carlsbad water, or, what I prefer and have used for years, a combination of sodium sulphate and phosphate or of sodium sulphate, phosphate, and bicarbonate. The salt is administered in rather hot solution on rising, subsequent to the lavage if this is practised; a small quantity of bitter infusion, such as quassia or calumba or of the tincture of nux vomica, taken coincidently, renders the saline draught better borne by the stomach and stimulates its passage into the bowel. Movement and breathing exercises should be taken after its ingestion, and no food is permitted for upward of an hour afterward. The solution should be drunk slowly and either in sips or in small draughts, at a few moments' interval, as its passage from the stomach is thus more rapid than if it has been hastily gulped. If the bowels are sluggish, and a tendency to looseness is not set up by the Glauber salt, I give a similar combination in smaller dose a half-hour before lunch and dinner, and on going to bed if food is not then taken. When sodium sulphate or phosphate is used more often than once daily and long continued, the dose should not ordinarily exceed gr. xx to ʒss of each. If hyperchlorhydria exists, sodium bicarbonate

[1] The crystalline salt is more laxative, containing a much larger percentage of sodium sulphate than the salt in powder form.

is omitted from the early morning combination, and a full dose (gr. xl to gr. lx) given either alone or in combination with a small quantity of Glauber salt or sodium phosphate three to four hours after the preceding meal and not later than one-half hour before the following one. The fluid extract of taraxacum or the succus taraxacum in 1-drachm to 2-drachm doses is coincidently administered.

Whatever the condition of the motor or secretory function of the stomach, notably good results are often obtained in cases of cholelithiasis by the daily morning use of strong sodium bicarbonate solution through the stomach tube, in the following manner: A funnelful (about 750 c.c.) of water at 105° to 110° F., containing two heaping teaspoonfuls of sodium bicarbonate, is passed into the fasting stomach, the intragastric extremity of the tube engaging the cardia (approximately sixteen inches); the funnel is held some distance above the head to obtain a douche effect. The stomach region from the fundus to the pylorus is massaged as the fluid enters, and subsequently for two to three minutes, after which the solution is siphoned off, and the stomach is douched once or twice with cool normal salt solution. The effect of soda thus used is beneficial in promoting a free outflow of bile into the bowel and in diminishing the viscidity of the bile. Should the bowels be acted upon too energetically, the stay of the soda solution in the stomach is lessened or the quantity of soda used diminished, and no saline laxative follows its employment.

Abundant out-of-door exercise, tennis, horseback-riding, and the like, except in case of very recent active symptoms, is insisted upon. Too energetic exercise is not permitted when there is persistent sensitiveness in the gall-bladder region or when there is a history of frequent recent attacks of colic. Energetic breathing exercises, general light massage, walking, hill-climbing, are all of utility in latent cases in stimulating the hepatic function and in obviating bile stasis.

If the trouble recurs despite carefully carried out treatment on these lines, and the patient is well-to-do and disinclined for operation—necessity for which not seeming too imminent—I advise a sojourn at Carlsbad. There, where business and family cares and social duties can be laid entirely aside and the life of the place becomes a pleasant incentive to recover health, much more may be accomplished on a similar regimen than at home. A woman patient with chronic cholecystitis whom I sent to Carlsbad three years ago, and who was rid of recurring attacks by two seasons there, received approximately the following course of treatment: Before rising in the morning it was customary to sip a tumbler of hot Sprudel water. Immediately after rising gentle exercise was taken, such as walking about and dressing, and in fifteen minutes a second tumbler was slowly drunk, followed by a third a half hour later. If the patient's strength permitted there was a considerable

interval (upward of an hour) before breakfast, during which a rather active walk was indulged in. Breakfast was commonly very light, such as toasted bread and tea, the latter without milk and sugar. This was followed in two hours by a more substantial repast—minced chicken on toast. Two hours later minced ham or chicken, with a purée of pea, potato, or spinach, was eaten. Three hours subsequently two tumblersful of cold Sprudel water were taken, with a lapse of a half-hour between, and in three-quarters of an hour after the second a meal similar to the last mentioned was indulged in. A tumblerful of Sprudel water was finally drunk before retiring. There were in addition the inevitable peat poultices applied to the hypochondrium. A good deal of out-of-door exercise was insisted upon. A number of small gallstones were voided while at Carlsbad. Quite a similar line of treatment, substituting the Priessnitz compress for the peat poultices, had been previously attempted here, but without much result, largely owing to the lack of earnest and persistent co-operation of the patient.

The object of treatment in these cases of calculous cholecystitis is not to promote expulsion of stones, but to dissipate the underlying catarrhal process and prevent its return, and, by maintaining persistent fluidity of the bile, to obviate further stone formation. Under the Carlsbad treatment and its modifications, however, small stones often are voided, leading the patient to imagine that he is thus rid of his trouble. If these calculi have not already engaged the cystic or common duct their passage from the gall-bladder is rather an unfortunate than a favorable circumstance, since the extrusion into the duct of a calculus too large to be readily if at all passed may be similarly favored.

The treatment of recent cases of stone in the common duct belongs to the physician, but for a short time only. Frequently the stone is passed into the bowel, entirely without treatment, a few days after the onset of colic. In other cases the calculus may linger in the duct despite all that is done to effect its dislodgement. In these cases of obstruction of the common duct, after the acute symptoms of obstruction have passed, I am in the habit of employing the sodium laxatives above mentioned and of resorting to the intragastric douche, with warm sodium bicarbonate solution and of high enemas of hot and cold normal salt solution, as before detailed, both for the purpose of reflexly favoring the onward passage of the stone into the bowel and of allaying the accompanying catarrh of the bile passages.

Formerly I was much inclined to the employment of olive oil in obstructions of the common bile duct by stone, and for several years used it rather freely, with results which apparently justified my confidence in this remedy. In recent years I have employed it but little, largely because of the constantly met with repugnance of patients to the remedy and because of the difficulty in its retention by the stomach

when administered in the full doses necessary—and also, perhaps, because I became skeptical of its utility, cases not infrequently occurring in which passage of the stone, because of its size, could not be thus influenced. In recently reviewing my notes of several cases of common duct obstruction in which I employed oil some years ago, and in which there followed cessation of colic and passage of calculi of fair calibre (in one case a triangular-shaped calculus the size of a beechnut was voided), I questioned if it was wise to entirely abandon this remedy. Naturally oil can be of no utility in case of massive calculus, but, considering the paucity of our remedies, it is worthy of at least brief trial in recent cases of obstruction of the common bile duct, for if it can be of no utility, its employment is unattended with harm. In searching for an explanation for the mode of action of the oil, presuming the result sometimes obtained is not entirely a *post hoc* one, it occurred to me some years ago its utility might rest on a sound therapeutic basis,[1] and that there seemed reason to suppose the effect attributed to the oil might be due rather to a product of its decomposition, glycerin. With unobstructed pancreatic flow it is not improbable that by virtue of the fat-splitting ferment steapsin a portion of the oil is disassociated in the duodenum into its components, fatty acids and glyceryl, and that nascent glycerin thus formed exerts in the duodenum an effect somewhat analogous to that which takes place when glycerin is introduced into the rectum—withdrawing water and causing hyperæmia, and causing irritation of the afferent nerves of the part with which it comes into contact, and thus leading to active reflex peristalsis. I believed that a similar effect might result from the presence of nascent glycerin in the duodenum as occurs from the introduction of glycerin into the rectum for its cathartic action. In my paper on this subject I remarked, in effect, that in addition to the active contraction which might be caused by the presence of glycerin in the duodenum, and which of itself would probably tend to contraction of the bile ducts and perhaps of the gall-bladder, the power of diffusion possessed by glycerin would perhaps enable it to enter the ductus communis, and even the hepatic ducts and the cystic duct, producing a similar depletion of the vessels there, and reflexly exciting the muscular fibres of these ducts to contraction. In consequence of this action an outflow of diluted bile would be favored which I thought would assist in expelling the stone. I said that since no other explanation is at hand as to the efficiency of the oil in these cases, and that, as is well known, glycerin is normally so formed from it in the bowel by aid of the fat-splitting ferment of the pancreas, and since it is probable that glycerin can produce the

[1] See my paper, A Suggestion as to the Action of Olive or Cottonseed Oil in Gallstone Colic: Observations on the Use of the Oils, and Report of Cases. The Medical News, November 23, 1889.

effects attributed to the oil, it may be not unlikely that these are due to glycerin thus formed. Rosenberg about this time reported he had found by experiments on dogs with gall-bladder fistula that large doses of olive oil greatly increased the quantity and diminished the consistency of the bile excreted.

After the publication of my paper suggesting this theory of the action of the oil, glycerin was suggested in the treatment of cholelithiasis. If the utility of glycerin is in the manner I proposed, unless it could be immediately brought into contact with the duodenum without a stay in the stomach it would be useless as a remedy. Some trials which I later made with it in impacted gallstone were resultless.

Olive oil employed in the manner outlined in my paper is certainly worthy of a trial in recent cases of common bile-duct obstruction by stone.

Preparatory Treatment before Operation in Cases of Obstruction of the Common Duct by Stone. Although this subject belongs rather to the surgeon, a few remarks concerning it here are apt, because of its extreme importance. It is well known that with cholæmia resulting from persistent obstruction of the common duct, and especially in cases in which there is coincident disease of the pancreas, there often exists a malignant hemorrhagic tendency which, unless strenuous efforts are made to overcome it, may readily terminate life after operation.[1] In order to obviate as far as possible this condition an effort should be made to re-establish a flow of bile and pancreatic juice into the bowel and to assist in the elimination of the bile already in the blood and tissues. The line of treatment suggested in cases of impaction is of value here. I do not refer to the use of oil, but to the employment of daily lavage with hot soda solution and to the use of high enemas of hot and cold water, as detailed in the case of Miss D. B. These last in former years were in vogue in the treatment of simple catarrhal jaundice, and are often of singular efficiency in promoting reflexly a flow of bile into the bowel. Lavage with soda solution acts similarly and perhaps also directly by diminishing the duodenal and bile-duct catarrh. The laxative sodium salts are also employed for a similar purpose, as outlined previously in discussing the treatment of cholecystitis in the interval. With these, taraxacum in full doses is prescribed. A morning laxative dose only of sodium phosphate and sulphate may be administered, and nitromuriatic acid and taraxacum given a half-hour

[1] This hemorrhagic condition may be related to pancreatic hemorrhage occurring in many cases of acute pancreatitis. There is good evidence to believe that although the cholæmia is an important factor, it is not the sole one in the development of the tendency to bleed after operation, so often encountered in gallstone cases. Mayo Robson states that his experience in increased number of operations on deeply jaundiced subjects, teaches him that there is much less danger of serious bleeding in patients jaundiced from gallstones than in those in which the jaundice depends upon pancreatic disease.

before the noon and evening meal and at bedtime. The results obtained in the case of impaction previously cited (Miss D. B.) under this treatment were quite remarkable, considering how firmly the large calculus was fixed in the common duct by adhesions. Bile appeared in the stools, and the amount of urine was enormously increased. If with this treatment the stools remain persistently clay-colored, there may be reason to suppose that the obstruction is other than by a calculus. To also assist in the elimination of bile by the urine, when the remedies suggested have had little effect in directly promoting its flow into the bowel, it is worth while to employ benzoic acid or one of its salts—sodium or ammonium benzoinate. However its mode of action, that benzoic acid has an effect in hastening the resorption of bile from the tissues, and its excretion is well established.

For a few days prior to operation, after discontinuing the above medicaments, calcium chloride should be administered, with a view to heightening the coagulating property of the blood, and if necessary, during or immediately subsequent to operation, parenchymatous injections of gelatin. The sterile solution of gelatin should always be at hand for immediate use.

It is highly important that, following operation for chronic obstruction of the common bile duct, treatment be instituted to obviate, as far as possible, the ill effects of the long-standing bile stasis. The imminence of hepatic cirrhosis in these cases must be borne in mind. Apart from this grave condition there usually exists thickening of bile ducts and often a chronic gastroduodenitis. In the liver structural changes have likely occurred, due to the long-existing back-pressure of bile and, often, to coincident infection. Even if not structurally damaged, liver cells long accustomed to the passage of bile into the lymphatics do not readily assume normal function, and despite the removal of obstruction and free passage made for the bile, bile still, for a more or less lengthy period, finds its way into the circulation. A continued observation of these cases is, therefore, of prime importance, in order to correct the gastric and bile-duct catarrh, to obviate further bile stasis, and thus to restore the liver, as far as possible, to normal function. The state of the kidneys must also be carefully looked to.

The after-treatment should be largely on the lines already laid down for the management of chronic cholecystitis. In addition, mention must be made of the utility of certain other remedies in cases in which the jaundiced hue of skin persists. Here, apart from the measures cited for the treatment of the catarrhal condition, and in addition to attention to general hygiene, exercises, baths, and local applications, I have found the persistent use of ammonium chloride and taraxacum of great service. I often alternate courses of ammonium chloride with nitro-muriatic acid. My usual mode of administering these remedies is to

employ a morning laxative of sodium sulphate or phosphate and to give diluted nitromuriatic acid (10 to 15 minims in taraxacum, fluid extract or taraxacum juice, 1 to 2 drachms) before the midday and evening meal and at bedtime. A course of ammonium chloride (grs. xv–xx, three times daily) is alternated with the acid, and this salt is similarly exhibited in taraxacum, but is administered from one to three hours after meals.

PERITONITIS OF THE DUODENAL REGION.

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We may consider the various peritonitides as having regional significance. Thus, peritonitis of the pelvic region, or of the right iliac region, present peculiar features by which they have long been recognized. It is with chronic peritonitis of the duodenal region, or, more properly speaking, with the plastic adhesions following peritonitis of this region, that this paper will deal, with the view of calling attention to certain peculiarities of this form of abdominal disease.

By the duodenal region we shall understand that portion of the abdomen, bounded posteriorly by the descending limb of the duodenum, the inner aspect of the upper pole of the right kidney, and the common bile duct; to the inner side, by the mesocolon; to the outer side, by the gall-bladder and liver; above, by the liver and gastroduodenal junction; and in front, by the hepatic flexure, border of the liver, great omentum, and abdominal wall. This space, which we may designate as the duodeno-hepatic fossa, is, next to the pelvis and right iliac fossa, most prone to peritonitis. Every surgeon is aware of the frequency with which he encounters the results of peritonitis in this region, in the adhesions which he so often discovers in attempting to expose the duodenum or the common bile duct.

Although there are peculiar features which characterize acute peritonitis of this region, it is rather the result of such an acute inflammation, which gives rise to the chronic disturbances which are less well understood, and which are of sufficient frequency and importance to merit the attention of the surgeon and internist.

The causes of plastic peritoneal deposits in this region are about the same as the causes of acute peritonitis. The three conditions which deserve pre-eminent mention as causative factors are cholangitis; cholecystitis, with or without gallstones; and duodenal ulcer, with or without perforation. For the completion of the etiological category,

however, may be added the following: duodenitis; round ulcer of the pyloric region; carcinomatous ulcer of the pylorus, of the hepatic flexure, of the gall-bladder, or of the liver; perforating gallstones; hepatitis; perinephritis; appendicitis; pericolitis.

The extent of peritoneal adhesions, resulting from these conditions, may be very variable. The disturbances which they cause, however, are dependent more upon the location of the adhesions and the degree of distortion of the relations of organs which they induce. Thus, adhesions between the hepatic flexure of the colon and the gall-bladder may be depended upon to give rise to two distinct symptoms; constipation and attacks of dragging pain in the right hypochondrium, induced by overloading of the colon. It is not difficult to define the symptoms of deep adhesions about the duodenum. It is easy to conceive of their dragging upon the gall-bladder and adjacent organs, and giving rise to disturbances due either to angulation of visceral canals or to attacks of pain and tenderness from tension. When food is emptied into the duodenum there is a reflex contraction of the gall-bladder, and if a stone prevents the escape of bile, at just that particular time there occurs the pain which is so characteristic of gallstone. I have seen the gall-bladder dragged down by adhesions to such a degree that the angulation at the beginning of the cystic duct was capable of causing an obstruction which, in its symptoms, quite simulated those of gallstone obstruction. More frequently, however, the symptoms are only those of tension or traction, and are especially noticeable when the patient stands or when the alimentary canal is loaded.

A vast category of conditions of this kind may be described, and the number of combinations which may be effected is very large. Thus there may be adhesions, binding the hepatic flexure to the duodenum, to the gall-bladder, to the liver, to the omentum, to the stomach or to several of these organs. The gall-bladder may be attached to the hepatic flexure, the omentum, the pylorus, the duodenum—one or all. The pyloric segment of the alimentary canal may be adherent to the gall-bladder, the colon, the liver, or bound down to the descending portion of the duodenum. These are only a few of the combinations which may be effected by these adhesions.

As a rule, these conditions give rise to no tangible symptoms. In many cases slight symptoms exist which are very apt to be attributed to some other cause. And in a certain number of cases the symptoms are pronounced and even alarming. The condition which seems to give the most evident symptoms is adhesion of the pyloric region or first portion of the duodenum to the gall-bladder, liver or descending duodenum, in such a way as to cause an angulation which is aggravated when the stomach contains food. As a result of this condition

the patient presents the symptoms of pyloric stenosis; and unless the condition is relieved by the giving or stretching of the adhesions or by operation, the degenerative changes in the mucous membrane and the musculature of the stomach incident to this may be looked for.

Hemmeter[1] refers to cases in which the stomach was of normal size when empty, but was abnormally dilated when filled with food. In these cases there was an angulation just beyond the pylorus. The distention of the stomach had caused this kinking by traction. I shall report below three cases upon which I have operated during the past year illustrating this obstruction of the duodenum.

When the contents of the stomach encounter an obstacle to their easy entrance into the duodenum, according to the recent writers on pyloric obstruction, a sequence of three changes takes place. First, there is insufficiency of muscular power to overcome the obstacle, and the stomach suffers from the retention of contents which should normally be expelled; second, a compensatory hypertrophy of the musculature develops, which may or may not be sufficient to overcome the obstacle; and, thirdly, in the event of muscular failure, atony and dilatation ensue, with the accompanying degenerative changes in the mucous membrane.

The stage of insufficiency is not marked in ordinary cases of benign stenosis. It may not be noticed until some error in diet precipitates an attack, due to the inability of the narrowed lumen to accommodate the mass of food. An attack of pain occurs, and is quickly relieved by vomiting. Just this condition may not be observed again for weeks or months. The narrowed or angulated duodenum or pylorus still exists; and the stomach is gradually undergoing the dilatation which merges into atony. Finally, the stomach becomes unable to empty itself of solid food, and distress is constantly present after eating. Constipation usually coexists. The disturbances arising from these conditions involve the great category of digestive and general nutritive defects incident to pyloric obstruction and stomach dilatation, with its accompanying atrophy and degeneration of the gastric mucous membrane, fermentation, ptomaïne poisoning, and inanition. Because of the absence of free hydrochloric acid in these cases and the presence of pyloric obstructive symptoms, malignant disease may be suspected. The differentiation should not be difficult. In the benign obstruction there is often a history of cholecystitis, gallstone, or peritonitis of the duodenal region. In carcinoma, the stomach-contents show more fermentation, more lactic acid, and more lactic acid forming bacteria; the progress of the disease is steady; rectal feeding does not improve the patient to the same degree; there may be the dissemination signs

[1] Diseases of the Stomach, 1900, p. 660.

of carcinoma; the bloody vomit and the presence of cancer cells all help to make the diagnosis. In the benign obstruction the cachexia is simply that of starvation, with the possible addition of ptomaïn poisoning; water can usually be taken; and while there is usually no tumor, still I have seen a case in which the hypertrophy about the pylorus, and the matting together of the structures in the duodenal region, together with the contraction of the upper part of the rectus muscle, gave the impression of a very palpable tumor.

C. A. Ewald[1] speaks of the possibility of old peritonitis giving rise to cicatricial bands or adhesions dragging down the pylorus in such a way as to give pyloric stenosis. Also Van Valzan and Nisbet,[2] after enumerating external causes of pyloric obstruction, say that it may be caused "by constricting bands of fibrous tissue, resulting from peritonitis." And for duodenal obstruction they also give local plastic peritonitis.

The following cases operated upon myself, in the service of Dr. Pilcher in the Methodist Episcopal Hospital, serve to illustrate these conditions:

Case I.—R. E., male, aged thirty-six years. Well until three years ago. At that time, while living in Mexico, he had a fever with afternoon temperature of 41.5° C., lasting for two months. The liver was enlarged. There was no jaundice or pain. He became very weak and was confined to bed for four months. He recovered, and was apparently well until a year ago, when he began to have heaviness in the epigastrium and pain after eating. Later the pain was deferred for two or three hours after eating. These symptoms continued. He had to restrict his diet, and steadily lost flesh and strength. Seven weeks ago the pain suddenly became worse, and he was able to take only fluids after that time, but even these gave distress. Examination by Dr. Dudley D. Roberts showed atony of the stomach, absence of free hydrochloric acid, gastric stasis, and fermentation, tenderness over the duodenal region, and a dull sense of discomfort over the epigastrium and radiating to the right side. It was Dr. Roberts' judgment that the man was suffering from atonic gastritis and gall-bladder disease.

Operation. Duodenal region exposed by vertical incision through the outer border of the rectus muscle. Adhesions discovered connecting gall-bladder and neighboring under surface of liver to duodenum, omentum, and pyloric end of stomach. The common duct, cystic duct, and region of the transverse fissure were covered with adhesions. The gall-bladder was enlarged, distended, and adherent to the first portion of the duodenum. Its walls were apparently normal. No stone. The adhesions were divided to permit deeper exploration of the duodenohepatic fossa. The gall-bladder was opened, but the entrance to the cystic duct could not be discovered. With the collapsed gall-bladder out of the way the stomach was permitted to drop back into its normal position. Abdomen closed with a small tube in gall-bladder to drain

[1] Diseases of the Stomach. [2] Ibid., 1898.

off bile for a few days. Patient fed on peptonized milk for ten days, then other fluids. No solid food until the end of three weeks. At first the fluids caused some of the old distress. This gradually subsided, and when solid food was taken it was enjoyed. The patient was discharged at the end of four weeks able to take full meals of solid food without pain or discomfort, and steadily gaining flesh and strength.

The tropical fever from which this man suffered was probably complicated by angiocholecystitis with a spreading infection to the adjacent peritoneal surfaces. There were two pain-producing conditions—distortion of the beginning portion of the duodenum, causing angulation and obstruction; and dragging down of the gall-bladder, causing obstruction to the escape of bile by angulation of the cystic duct.

Case II.—Male, aged fifty-two years. First symptoms began five years ago with pain referred to the stomach. This pain and feeling of discomfort in the epigastrium was almost constant. It was worse about half an hour after eating, and quickly relieved by vomiting. This continued for three months. He then placed himself under medical treatment and was much improved. Four years ago the same disturbances after eating returned, and have steadily grown worse. At the time of his admission to the hospital the pain after eating was severe. When the stomach was empty there was no pain. During the past four years he had lived almost exclusively on fluids. Solid food gave so much distress that he had desisted from taking it. For the past two years he had been failing in strength, and during the last year he had lost twenty pounds in weight. The symptoms were distinctly referable to obstruction to the passage of food from the stomach into the intestine. Bowels constipated.

Examination. Strongly built man. Abdomen thin-walled, scaphoid. Everywhere there is increased muscular rigidity. The most tender spot is just to the right of the middle of the epigastrium. Some tenderness to the left of the middle line. After eating the pain is referred to the right of the middle line. Board-like rigidity, giving a sense of tumor at this place. Absence of free hydrochloric acid.

Operation. Duodenal region exposed through vertical cut through outer border of rectus. Bands of adhesions connecting gall-bladder, stomach, and hepatic flexure were exposed. These adhesions had fixed the pyloric end of the stomach in such a position as to cause an angulation of the duodenopyloric segment of the alimentary canal, and thus a partial obstruction. These were divided and the above structures permitted to separate, exposing the descending duodenum, covered by the most dense adhesions. The gall-bladder was not thickened. The peritonitis which caused these adhesions had evidently originated from the duodenum. In this case a thickening, just inside of the pylorus, could be felt in the stomach wall; and to determine its character, the stomach was opened by a longitudinal incision, and the mucous membrane over the mass found perfectly normal and freely movable. I am not sure but that this was an hypertrophy similar to that of "stenosing gastritis" or "hypertrophic stenosis" of the pylorus, first described by Cruveilhier and Andrae. Although it was more of a localized patch of thickening, apparently in the muscularis. However, the wound in the stomach was closed transversely to its long axis to

relax and compensate for any obstruction which this might have caused. The stomach dropped back into its normal position when the adhesions were liberated.

Rectal nourishment alone for five days. Then fluids were given by mouth, and the diet rapidly increased. On the fourteenth day solid food was taken with great relish and with perfect comfort for the first time in four years. By the end of three weeks he was allowed to take full meals of meat and vegetables, which he enjoyed without disturbance. Three months after his operation he was still perfectly well.

The most probable origin of this man's trouble was in a peritonitis transmitted through the walls of the duodenum, probably from ulcer.

Case III.—Woman, aged thirty-one years. Trouble began two years ago with aching pain in the stomach after eating, lasting one or two hours. Nausea; no vomiting. She often noticed blood in the movements. This disturbance varied in intensity until six months ago, when she had a particularly severe attack lasting three weeks. This was characterized by pain in the epigastrium, coming on at variable intervals after eating from half an hour to two hours or more. The pains were cramp-like and cutting.

Examination of the stomach showed tenderness over whole organ, but especially at the pyloric region. The patient had been under treatment for gastric ulcer for three months with large doses of bismuth, bicarbonate of soda, peptonized milk diet, and rest in bed. Under this treatment the pain and tenderness had steadily subsided. She was fairly comfortable after getting up, but as soon as solid food was taken it precipitated another attack of pain. There was usually pain under the right shoulder-blade. The chief tenderness was over the duodenum. The gall-bladder was not tender. The history pointed strongly toward ulcer of the duodenum with peritoneal adhesions of the duodenal region.

Operation. Abdomen opened by cut separating fibres of right rectus muscle over duodenum. Rather extensive adhesions between gall-bladder, stomach, colon, and duodenum were found. The pyloric end of the stomach was bound closely to the gall-bladder and liver, causing a distortion of the duodeno-pyloric canal. These adhesions were divided and the stomach exposed and permitted to fall back into normal position. The adhesions were most dense about the duodenum and at the base of the gall-bladder. The gall-bladder was not thickened, and seemed normal except for the above-mentioned adhesions, and the fact that it contained thirty small stones without facets. These were removed. The bile-contents of the gall-bladder were normal.

The patient was allowed solid food at the end of seven days, and it was taken with great relish, and without any distress. After that the diet was increased until she was able to eat heartily and enjoy ordinary food without pain or dyspepsia.

In this case the later symptoms were accounted for by the distortion of the alimentary canal and its fixation by the periduodenal adhesions. The most dense adhesions were about the duodenum. It seems most probable that the peritoneal irritation which gave rise to these adhesions was of duodenal origin. Just what the relation to the sup-

posed duodenal ulcer may be, it is difficult to say. I believe that the gallstones had little or nothing to do with the symptoms.

It is reasonable to assume that these patients represent types of a large class of cases which have not received the study which their frequence and importance should demand. I am convinced that many of the cases of vague and intractable gastro-intestinal disturbances belong to this class. If the mechanical distortion of the alimentary canal is not corrected, a long chain of chronic digestive discomforts ensue.

Two questions remain to be settled: What will time and the yielding of adhesions do for these cases? and what has surgery to offer? The first question is difficult to answer because of the difficulty of making a positive diagnosis without operation. That surgery offers relief to these cases the above reports would tend to show; although in all of these new adhesions will certainly form. The operation can only liberate the parts from their disturbed relations, and place them in such position that it may be hoped that the new adhesions shall be less vicious than the old.

A CONTRIBUTION TO THE STUDY OF THE HUMAN BLOOD PRESSURE IN SOME PATHOLOGICAL CONDITIONS.*

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It is only within the last few years that the study of the arterial blood pressure of the human economy in its relation to clinical pathology has been investigated at the bedside, or allotted a space in textbooks of medicine. The chief reasons for this are, perhaps, the following: 1. The intricacy and complexity of the whole subject of blood pressure, which, even in a healthy individual, fluctuates more or less continually and is influenced by so many and diverse causes. 2. The difficulty of estimating the pressure with sufficient accuracy and rapidity to make the investigations statistically useful and clinically practical.

A number of instruments have been devised in an attempt to fulfil the foregoing requirements which may be classified thus:

1. Those which estimate the pressure by noting the return of color to the skin, which has been previously rendered anæmic by pressure—*e. g.*, Gärtner, von Kriess, Marey.

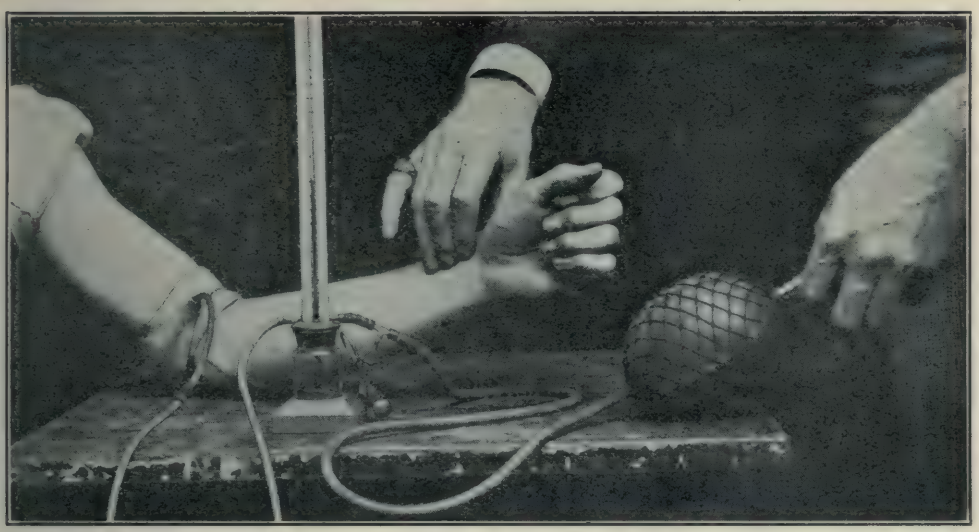
2. Those which gauge the pressure, using as a standard the amount of compression necessary to obliterate the distal pulse in the arm or leg—*e. g.*, Riva-Rocci, Vierordt, von Basch.

* Read before the College of Physicians of Philadelphia, Feb. 9, 1903.

3. Those fashioned like the instruments of Mosso and Barnard and Hill, which select the point of greatest arterial oscillation as the pressure index.

The following observations were made upon cases at the Pennsylvania Hospital, occurring in the services of Drs. Morris J. Lewis, Frederick A. Packard, Alfred Stengel, and J. A. Scott.

The readings were taken from the right arm of the patient, on different days, but as nearly as possible at the same hour of the day and in the same (usually recumbent) posture. The instrument used was that designed by Riva-Rocci, who, upon making comparative tests upon animals coincidently with it and with a manometer directly connected with the arterial stream, found the readings to closely correspond; those of the manometer being pretty constantly from one to two cubic millimetres of mercury lower.



The Riva-Rocci hæmodynamometer.

The investigations of Perthes and Hensen have corroborated these results. The latter finding in experiments on the cadaver close accuracy in the readings, "provided there was no rigor mortis or œdema" present. It is only fair to add, that all observers have not found such equally good results; but, on the whole, those obtained with this instrument by different investigators, when compared to the actual manometrical pressure, have shown fewer discrepancies than has been the case with other forms of apparatus.

The Riva-Rocci instrument consists, as is shown in the accompanying photograph, of a hollow rubber cuff, rendered outwardly inexpansile by a snugly fitting covering of muslin and a metallic band. The interior of the cuff communicates by means of rubber tubing with a manometer and a syringe bulb. When in use the cuff is slipped over

the hand, applied to the arm just above the elbow, adjusted approximately to the size of the arm, and secured. Sufficient air is then pumped into it to occlude the radial pulse, and as soon as this is accomplished the air is gradually allowed to escape until the arterial impulse is once more perceptible to the palpating finger at the wrist, at which point the reading is taken from the manometer scale in mm. of Hg.

Reflection leads one to the belief that the condition of the soft parts —thickness of the skin, muscular tonus, density of the arterial wall, etc.—must have more or less effect on the accuracy of the readings. However this may be, there can be no doubt of the value of sphygmanometric observations in comparing the fluctuations of pressure in the same individual; and it may be asserted with equal certainty that by carefully selecting individuals for purposes of comparison, and having a sufficiently large number of cases under observation, conclusions may be drawn probably not much at variance with actual existant conditions.

Just as the study of thermometry, though known at an earlier date, lacked utility until Wunderlich, from a large number of statistics, was able to establish its importance in clinical medicine, so it is only by repeated observations carefully made and frequently repeated that we can hope to derive diagnostic or prognostic aid from the study of blood pressure; a subject still relatively in its infancy, and one which is not only replete with interest but of the greatest importance in all vital phenomena.

The *normal pressure* as indicated by the Riva-Rocci apparatus is, according to Gumprecht, 140 mm. for men and 120 mm. for women, while Hensen's estimate is 137 mm. and 132 mm. The figures here appended are the pressures recorded of a healthy man, aged twenty-seven years, in the sitting posture under approximately similar circumstances upon different days, and show a marked tendency to uniformity: 120, 108, 122, 118, 132, 134, 130, 130, 125, 125, 120.

Physiology. It may not be amiss to consider cursorily a few of the more important factors concerned in the maintenance of physiological blood pressure.

Primarily arterial pressure (for practically we may overlook that of the venous system) can be said to depend upon:

1. The force and frequency of the cardiac contractions.

2. The amount of resistance in the bloodvessels, which is chiefly determined by: (*a*) The vasomotor centre in the medulla; (*b*) the state of the splanchnics; (*c*) peripheral sensory reflexes acting through the medullary centre; (*d*) the state of the muscular system.

3. Respiratory movements—inspiration increasing and expiration

decreasing the tension—which is in turn accomplished by: (*a*) The tension and velocity of the lesser circulation; (*b*) the suction of the large veins; (*c*) the intra-abdominal pressure; (*d*) the contraction of the heart; (*e*) nervous stimulation.

4. Posture—different observers have arrived at opposite conclusions: some asserting that pressure is highest when recumbent and lowest when erect, others that the reverse is the case.

It is a well-known fact that blood pressure varies more or less constantly, not only in different, but even in the same individual. In addition to variations due to such well-recognized causes as posture, gravitation, exercise, altitude, temperature, digestion, etc., periodic fluctuations of but a few seconds' duration and of sufficient intensity to cause in rabbits an increase of 20 mm. to 30 mm.—Traube's waves—are observed. This variation of pressure is based upon a periodic diurnal fluctuation, and, like the pulse rate, the secretion of urine, the elimination of CO_2, etc., rhythmically recurs independent of the ingestion of food, and bearing no apparent relation to cardiac or respiratory activity.[1] It is usually highest during the afternoon and sinks toward evening (Hensen). That such fluctuations in tension occur in man has been shown by Mosso[23] and von Pfungen.[16] Zadek[2] gives the average daily fluctuation, from different causes in man, as from 8 mm. to 15 mm. Blood pressure also differs according to sex and age, being lower in women than in men; and lowest at birth, from which time it steadily increases until maturity is reached.

Manifestly, as a result of the cardiac contractions, three different states of blood pressure must exist: the systolic (highest), the diastolic (lowest), and the mean pressure. The latter is, of course, the most important, because upon it depends the hæmic velocity; nor is its relation to either of the two first mentioned pressures a constant one. For example, the mean pressure would be much nearer the systolic pressure in a case of mitral stenosis, in which the volume of the pulse is small and the pressure high, than in aortic insufficiency, in which the volume is large and the tension low.

Since the completion of my observations a modification of the Riva-Rocci apparatus has been completed, through which by means of an indicator and a recording drum the whole pressure curve can be graphically reproduced. Owing to the lack of such an instrument I have had to content myself with obtaining records of the systolic pressure, a method which, while, as has been said, it is open to objections, yet may in the majority of cases be looked upon as a fairly reliable index.

The *normal amplitude* of the pulse wave is given by Hensen[3] as ranging from 5 mm. to 20 mm. of Hg. The same author gives as the limits

within which human life is possible from 70 mm. to 266 mm., though he has recorded one case in which life was sustained for a short time with a pressure of only 55 mm. The largest diurnal variations occurring in a healthy man have, I think, been reported by Burkhart,[4] who found in an individual a difference of 40 mm.; the pressure being highest at 1 P.M. and lowest at 3 P.M.; and by Hensen who noted a daily fluctuation of 50 mm. Cook[24] has found the lowest pressure between 3 and 4 A.M.

It is generally conceded that while abnormally high pressure may be borne for a long time without seriously interfering with the vital functions, abnormally low pressure if it continues for any length of time usually means death. In this connection Cushing[5] has pointed out the fact that by regularly charting the blood pressure during anæsthesia the oncome of shock may be anticipated and prevented in the course of surgical procedures.

With regard to the process of *digestion*, Columbo, Weiss,[17] and von Recklinghausen[6] have found the pressure to be highest just before the midday meal, with a gradual fall while digestion was in progress. The well-known irritability of animals and human beings, when the dinner hour is delayed or missed, may bear some relation to this increase of arterial tension; for it is also known that people who suffer from gout (and are usually irascible) and from agitated melancholia (*vide* Alexander, *Lancet*, July 5, 1902) are usually the subjects of a tense arterial wall.

The influence of *psychic activity* is a potent one. Von Recklinghausen noted in his own person an increase of 14 cm. of water when someone entered the room with whom he desired to speak. Gumprecht[7] found an increase of pressure to be produced by anger and scolding, which again corresponds to the tendency of apoplexy to occur during fits of rage.

Von Basch[8] has reported a series of 120 cases, with hypertension, of whom 7 died of apoplexy; and Hensen 12 cases, of which 6 were similarly afflicted. I have observed in my own radial artery an increase of 10 mm. of Hg produced by carrying on an animated conversation.

Muscular exertion causes an elevation of blood pressure, but if it be carried on until cardiac fatigue supervenes it again falls and eventually becomes subnormal (Schott[18]), an admirable conservative process on the part of nature by which acute cardiac dilatation is avoided.*

The *normal range* of tension, as shown by the Riva-Rocci instrument, lies between 100 mm. and 160 mm. No definite relation has as yet been

* For the discussion of the means by which this is brought about the reader is referred to Guntz's article, "Handbuch der Physik. Therap.," Band ii., Th. I.

established between pulse rate and blood pressure, nor is it uncommon to find the latter higher in the right arm than in the left.

Pathology. The lowest pressure met with is usually seen in shock, in convalescence from fevers, in acute cardiac asthenia, in cachexia, and in the agonic periods. The highest limits of tension are, as a rule, observed in cases of chronic interstitial nephritis, either with or without arterio-sclerosis. Hypertension is much more common than hypotension, which has usually a more serious portend; and all observers agree that pre-agonic fall of pressure does not occur long before death itself supervenes.

According to Hensen, cases with a pressure below 70 mm. terminate fatally; and even though the tension fall but as low as 90 or 95 mm. and be accompanied with untoward symptoms, a bad prognosis is augured.

In several cases I have seen a rise of 10 mm. to 15 mm. accompany the occurrence of paroxysmal *pain*, and disappear with subsidence of the attack. Such an event was observed in two cases of saturnine colic, and in one case of hypertrophic hepatic cirrhosis. In these cases the rise of tension was probably due to vasoconstriction resulting from stimulation in the medullary centre, produced by peripheral sensory impulses.

Potain[19] states that as a general rule *low tension* occurs in typhoid fever, pulmonary tuberculosis, and in acute and chronic articular rheumatism.

Moderate tension in pneumonia, pleuritis, febrile gastritis, chlorosis, hemorrhages, organic heart lesions, and in diseases of the arterial system.

Very high tension in interstitial nephritis, arterial atheroma, and in diabetes.

According to Oliver,[20] hypertension is observed in certain neuroses, chronic goutiness, renal disease, heart disease of peripheral origin, irritable skin affections, anæmia, obesity, and endarteritis.

As will be seen from the following table of cases of enteric fever, the blood pressure tended to be subnormal throughout the whole course of the disease, it being highest during the fastigium and lowest during convalescence. That the higher pressure noted in the former state was not due merely to increased temperature is shown by Case No. 21, in which relatively high pressure existed with little fever, and in Case No. 26, in which the reverse condition obtained. These results accord pretty closely with those of other observers, it having usually been found that pressure rises with temperature, but falls if the fever be long continued (Arnheim[9]), or if cardiac weakness is present (Zadek[2]). How deceptive may be the tactile sensation was shown by a number of

cases in which the pulse was described as very soft and dicrotic, whereas by actual measurement it was found to be of higher tension than later in the disease, when the sensory impression of weakness was less marked. Observations were made upon a much larger series of cases than have here been tabulated, and in a number, measurements were made upon the same patient every few days throughout the course of the disease, but the findings were of such uniform character that further tabulation has seemed unwarranted. No definite relations could be established between pressure and prognosis, either as regards the eventual outcome or concerning the likelihood of hemorrhage or perforation to occur.

Potain[19] has pointed out the fact that a prolonged fever with blood pressure persistently subnormal should make us strongly suspect typhoid fever.

TYPHOID FEVER.

No.	Name.	Sex.	Age.	Press.	Pulse.	Resp.	Temp.	Stage of disease.	Remarks.
1	L. B.	M.	10	110	100	28	102°	Incipient.	
2	A. S.	M.	30	115	80	24	100	"	
3	A. W.	M.	36	118	88	24	101	"	Ill four days.
4	J. C.	M.	18	105	88	24	101	"	Ill eight days.
5	2171	M.	20	130	92	24	101 2/5	"	Malaise eight days First day in bed.
6	B. C.	M.	25	125	80	24	104	"	Malaise two days. First day in bed.
7	2677	M.	16	98	100	26	102	"	
8	T. H.	M.	28	139	96	24	102	Fastigium.	Very robust man.
9	K. K.	F.	31	112	130	26	104	"	
10	B. B.	F.	24	132	118	26	102	"	
11	V. P.	M.	28	101	90	26	102	"	
12	C. L.	M.	25	125	96	24	102	"	
13	J. H.	M.	17	108	90	24	100	"	
14	J. N.	M.	19	100	102	24	99	Defervescence.	
15	M. D'F.	M.	18	118	72	24	99 2/5	"	Slight attack.
16	A. E.	M.	50	95	84	24	98 4/5	"	Severe illness.
17	D. O.	M.	29	106	72	24	100	"	Slight attack.
18	F. F.	M.	19	98	76	20	100	"	" "
19	M. T.	F.	32	108	98	24	99	"	
20	S. W.	M.	10	92	108	24	99 3/5	"	
21	P. R.	F.	24	135	90	24	98 4/5	"	
22	M. A.	M.	17	118	60	24	98	Convalescence.	Moderate attack.
23	J. H.	M.	17	102	88	24	98	"	Slight attack.
24	S. F.	M.	27	109	74	24	98 2/5	"	Moderate attack.
25	J. C.	M.	14	95	70	22	97 3/5	"	Severe attack.
26	F. S.	M.	30	96	128	24	103	Relapse.	
27	P. W.	M.	29	106	88	24	98	Convalescent.	
28	J. K.	M.	24	93	56	20	96	"	

Two cases of *paracolon* infection which were under observation from time to time during the course of the disease showed low tension—117, 110—during the fastigium, and still lower readings during convalescence.

For a more comprehensive and detailed study of the blood pressure in typhoid fever, the reader is referred to the careful analysis of 150 cases by Alezais and François.[10]

CROUPOUS PNEUMONIA.

No.	Sex.	Age.	Press.	Pulse.	Resp.	Temp.	Remarks.
431	M.	30	130	84	48	100	Urine—albumin and casts.
523	M.	50	145	112	40	102	Arterio-sclerosis; parenchymatous nephritis.
549	M.	34	125	84	24	98	
725	F.	23	130	74	24	98	
976	F.	37	100	102	24	103	Two days before crisis.
431	M.	30	130	80	48	98 2/5	Lysis.
310	M.	40	115	64	24	98	
	F.	8	105	120			
	F.	34	165	68	...	...	Double mitral disease; miscarriage twelve hours before.
	F.	27	115	106	28	102 3/5	

The causes which influence arterial tension in croupous pneumonia are even more complex than in other fevers. As will be seen from the foregoing table no constant relations seem to exist. In nearly all the cases readings were made before and after the crisis. In Case No. 523 a critical drop of 15 mm. occurred, but the remaining cases showed only slight variations. Zadek[14] has reported three cases of pneumonia in which, at the time of crisis, pulse temperature and tension fell coincidently; and Christeller[21] with the von Basch instrument has recorded a drop of 40 to 50 mm. after the crisis of high fevers. The discrepancy between my results and those just mentioned may, perhaps, be due to the fact that the pressure was in some cases not taken until two or three hours after the temperature had fallen. In considering the state of the blood pressure in this disease it must be borne in mind that, as H. C. Wood, Jr.'s[22] experiments have demonstrated, blood tension in the lesser and in the greater circulation are not necessarily coincident—hypertension may exist in the systemic circulation, the pressure in the pulmonary arteries being at the same time normal, and *vice versa*.

NEPHRITIS. In the *interstitial variety* of this disease the blood pressure was found uniformly above the normal, in some cases extraordinarily so; and, while many of them were complicated by arterio-sclerosis, several occurred in individuals in whom this condition was at least not recognizable to the touch. In none of the cases here tabulated was there present any œdema of the arms which could add to the apparent height of the pressure. All the cases observed in uræmic coma had very high tension. In a number of instances fall of pressure, under treatment, was accompanied with a diminution of albuminuria and well-marked amelioration of symptoms. These facts are corroborated by the investigations of Carter,[12] who found the mean average pressure in this variety of nephritis 62 mm. higher than in acute nephritis. The foregoing results, moreover, accord closely with

the findings of nearly all investigators, as well as with facts clinically long well known.

CHRONIC INTERSTITIAL NEPHRITIS.

No.	Name.	Sex.	Age.	Press. c.m	Pulse.	Remarks.
1	T. B.	M.	40	175	90	
2	T. C.	M.	49	235	65	Pressure fell under treatment to 168, the albuminuria coincidently decreasing.
3	S. T.	F.	54	250	84	Death from uræmia. Autopsy confirmed diagnosis.
4	A. V.	F.				
5	A. Z.	M.	50?	250	104	Death from uræmia.
6	F. P.	M.	37	165	76	
7	E. N.	F.	60	164	70	Arterio-sclerosis.
8	P. Y.	F.	49	250	68	Slight arterio-sclerosis.
9	H. G.	M.	45	210	70	Arterio-sclerosis ; valvular heart disease.
10	D. D.	M.	63	225	124	Arterio-sclerosis.
11	J. R.	M.	...	160	...	Myocarditis.
12	J. S.	M.	24	220	92	Retinal hemorrhages. Under treatment pressure fell to 162, with a coincident decrease in albumin. Died, after Edebohls' operation, from uræmia.
13	398	M.	50	180	70	
14	699	M.	58	166	64	Had had two attacks of angina pectoris.
15	1915	M.	58	175	70	Marked nodular arterio-sclerosis ; myocarditis.
16	3618	F.	62	224	80	Marked arterial thickening.
17	3787	F.	72	190	100	Marked sclerosis; right-sided hemiplegia nine months before.
18	557	M.	45	160	100	
19	S. L.	F.	57	285	80	Marked atheroma ; hemiplegia.
20	A. F.	F.	62	260	88	
21	A. V.	F.	60	185	88	Arterio-sclerosis ; organic heart disease.

Most observers have found an approximately normal arterial tension in *chronic parenchymatous nephritis.* The few results here tabulated of this disease show a decidedly subnormal pressure, which is probably in part due to the poor physical condition of the patients, but certainly indicate an enormous difference between this condition and that arising from contracted kidneys.

CHRONIC PARENCHYMATOUS NEPHRITIS.

No.	Name.	Sex.	Age.	Pressure.	Pulse.	Remarks.
1	M. M. . . .	M.	25	103	80	
2	P. A. . . .	M.	45	100	68	
3	M. B. . . .	F.	39	105	116	Tachycardia.
4	D. E. . . .	F.	23	122	88	Mitral insufficiency.
5	R. S. . . .	M.	45	115	72	
6	W. E. . . .	M.	39	110	88	
7	D. P. . . .	M.	18	120	80	
8	2642 . .	M.	52	140	108	

ARTERIO-SCLEROSIS. It is, of course, impossible to draw an absolute line between sclerotic and non-sclerotic arteries by the unaided tactile sense unless the condition is well advanced. Again, in the results obtained much will depend upon the location of the greatest arterial thickening. Thus, pressure will be much higher if the splanchnics or the small systemic vessels are involved than if the former are relatively normal or the induration chiefly confined to the larger arteries. The

following observations were made upon cases in which well-marked radial sclerosis was present, in patients in whom so far as was ascertainable no other determining pathological condition existed. In considering the results, allowance must be made for a certain amount of error, arising from the resistance to compression, of the stiffened arterial wall itself. This resistance has been estimated by von Basch at 5 mm. as a maximum for the radial. Hensen's figure, based on rather unsatisfactory reasoning, is 20 mm. for the human brachial artery. So far as I know no conclusive experimental work has been done on the subject. The problem is certainly a complex one, for co-existent with arterial degeneration a variable amount of myocarditis and nephritis is usually present, each of which conditions are notably accompanied by high tension. The fact that some cases of marked arterio-sclerosis have an approximately normal pressure would rather seem to indicate that the stiffness of the vessel wall cannot have much effect upon the height of the tension recorded.

ARTERIO-SCLEROSIS.

Name.	Sex.	Age.	Pressure.	Pulse.	Diagnosis.	Remarks.
E. E.	F.	78	218	84	Fracture of femur.	Arterio-sclerosis very marked.
E. M.	F.	60	222	80	Infected wound of leg.	" " marked.
S. M.	F.	70	168	66	Fracture of leg.	" " moderate.
M. M.	F.	80	185	88	Dislocation of shoulder.	" " marked.
E. N.	F.	60+	164	70	Vertigo.	Moderate arterio-sclerosis.

SATURNISM. The tendency of chronic plumbic intoxication to produce interstitial nephritis and arterio-sclerosis is well known. That the condition is usually accompanied by high arterial tension seems to be likewise accepted as a fact. Whether this occurs only secondarily after changes have been wrought in the kidneys and vessel walls, or whether the lead itself exercises a constricting action upon the vascular system, has not been definitely determined, though the evidence points toward the latter conclusion. In two such cases reported by Christeller[14] there was noted as the result of treatment a considerable (10 mm., 30 mm.) decrease of tension. A similar event occurred in a number of my cases in which the elimination of lead from the system and the decrease of blood pressure seemed to progress hand in hand. To be sure, rest in bed, the relief of pain, and the administration of potassium iodide—which Jodbauer[15] believes to be an arterial depressant—would of themselves account for a certain amount of vascular relaxation; but as the tension continued to diminish after the first two factors had ceased to be active, and as the power of the iodide to lessen pressure is not a great one, it would appear that the lead *per se* must exert a positive influence. Plumbic intoxication stands third in the

list of factors which produce high pressure; and, as Hensen remarks, "in a case continued of hypertension without demonstrable cause we must, besides arterio-sclerosis and chronic nephritis, investigate the possibility of lead poisoning."

LEAD POISONING.

Name.	Age.	Press.	Pulse	Resp.	Occupation.	Localization.	Attack.	No. yrs. at work.	Urine.	Remarks.
1943	21	185	80	20	In lead works.	Colic.	Second	1	Negative.	
J. B.	24	180	84	25	Painter.	Encephalopathy.	First	Unk.	Albumin.	
631	28	118	92	20	Painter.	Colic.	Second	10	Albumin.	Convalescent.
W. V.	48	194	58	18	Paint works.	Colic.	.....	...	Negative.	
486	36	150	80	24	Painter.	Colic.				
St.	48	142	60	32	Painter.	Wrist-drop colic.	Second	15	Trace alb.	
J. S.	36	150	74	20	Painter.	Colic.	Fifth	24	Trace alb.	
J. K.	21	148	90	20	Lead works.	Colic.	Second	...	Negative.	
A. A.	38	170	72	24	Hide dyer.	Colic.	Second	...	Negative.	

HEART DISEASE.

No.	Name.	Sex.	Age.	Press.	Pulse	Remarks.
1	W. R.	M.	18	112	100	Mitral regurgitation and stenosis.
2	M. H.	M.	23	128	90	" " " "
3	G. L.	M.	45	122	80	" " " "
4	B. F.	F.	30	142	64	" " " "
5	G. McM.	M.	35	125	100	Mitral regurgitation and stenosis; pericarditis; parenchymatous nephritis.
6	W. McL.	M.	20	108	84	Aortic and mitral insufficiency.
7	S. G.	M.	16	120	115	Aortic insufficiency, hypertrophy, adherent pericardium.
8	L. C.	F.	40	120	100	Mitral and tricuspid insufficiency.
9	C. F.	F.	37	145	100	" " " "
10	J. K.	M.	50	135	94	Mitral and aortic insufficiency.
11	P. H.	M.	13	88	...	Mitral stenosis.
12	401	F.	39	105	116	Tachycardia, neurasthenia.
13	W. L.	M.	50	166	72	Angina pectoris twenty-four hours after attack.
14	J. M.	M.	22	117	106	Pericarditis, endocarditis, pleuritis.
15	G. B.	M.	42	180–80	...	Myocarditis, nephritis.
16	G. McM.	M.	35	115	98	Pericarditis, double mitral lesion.
17	M. C.	M.	38	138–115	68	Myocarditis, nephritis.
18	A. de B.	M.	26	125	128	Pericarditis, femoral thrombosis.
19	A. M.	F.	25	128	64	Mitral insufficiency.
20	753	M.	13	92	90	Acute endocarditis.
21	1641	M.	30	104	52	Acute endocarditis, due to B. typhosus; no intestinal lesions.
22	428	M.	20	100	84	Aortic and mitral insufficiency: pulmonary embolism.
23	Z. P.	M.	35	130	116	Mitral insufficiency and stenosis.

Considering the wide limits within which functional variations of tension may occur, it is hardly strange that still greater fluctuations should exist in cases of organic lesion such as are met with in cardiac disease. Certainly it is a fact, that, as remarked by Potain in his book on *Sphygmanometry*, "in cardiac disease we will find great variations of pressure." This applies not only to the differences of tension which

occur in contrasted individuals suffering from the same malady, but refers as well to the marked daily and hourly fluctuations which are seen in the same person. The cases here tabulated are, of course, too few, too diverse, and too much complicated by co-existent pathological conditions to alone furnish a basis for deductions, but from a study of them, together with an investigation of all the literature upon the subject which has been at my disposal, the following statements concerning heart disease seem warranted:

1. Daily and hourly variations of tension are commoner and greater in amount than in health or in other afebrile pathological conditions unaccompanied by heart disease.

2. In *mitral insufficiency* the pressure is usually normal, it may be subnormal, but is rarely supernormal in uncomplicated cases.

3. In *mitral stenosis* tension tends to be higher than in insufficiency, and when both lesions are present it tends to be higher than when the latter condition alone exists, provided that compensation is fairly good.

4. In *aortic insufficiency*, especially if compensation is good, the systolic pressure is above normal, often markedly so. The wave amplitude is much greater than normal (one of Hensen's cases showed a systolic pressure of 150 mm. and a diastolic pressure of only 50 mm.). The greatest amount of daily individual fluctuation occurs in this variety of heart disease. The pressure does not fall below the normal unless the lesion is complicated by mitral disease or myocarditis (Potain).

5. *Myocarditis* is usually accompanied by high tension, and cardiac *dilatation* by low tension.

6. No constant relation exists between *pulse rate* and blood pressure.

It is doubtful if any rules can be laid down as to the relation of arterial pressure to the integrity of compensation. Potain, it is true, believes that in a general way the more nearly tension approaches the normal the better will it be, but this statement is, to say the least, open to many exceptions, and in numerous ones of my cases this was by no means the case. The above-mentioned author asserts that in heart disease a fall of pressure is always an unfavorable sign; this is, of course, especially the case when dilatation exists, and has been substantially exemplified through the careful researches of Schott,[21] who, in the course of his Nauheim treatment, has produced demonstrable diminution of cardiac dilatation, and has showed this to be coincident with an increase of arterial tension and of physical well-being.

The following table is fairly illustrative of the diurnal fluctuations which commonly occur in cardiac disease. The patient was during the greater part of these observations in bed, and taking small doses of glonoin, the administration of which, so far as sphygmanometry would indicate, was uncertain in its effects. This test of the therapeutic efficacy of the drug is not a fair one, inasmuch as the dosage

was small and infrequent, and because the observations were made without any constant relation to the time of its administration.

MITRAL STENOSIS.

Observations on different but not always consecutive days.

142	175	155	150	150	135	132	140 (erect)	120	130 (erect)	120 (erect)

The foregoing pressure readings were made upon a woman, aged thirty-eight years, who had had numerous attacks of rheumatic fever, and in whom stenosis was marked and accompanied by some insufficiency.

A fact that must not be overlooked in sphygmanometrical observations upon cases of heart disease is, that we are in these particularly likely to err on account of the irregular force of the systolies.

MISCELLANEOUS CASES.

Diagnosis.	No.	Sex.	Age	Press.	Pulse	Resp.	Temp.	Remarks.
Catarrhal jaundice	417	F.	39	112	76	24	98°	
Cholecystitis	20, 38	M.	38	170	60			
Catarrhal jaundice	18, 81	F.	44	110	100			
Cirrhosis of liver	.....	M.	49	130	84	...	.....	Jaundice, nephritis.
Emphysema	21, 21	M.	65	120	86	20	$98^{4}/_{5}$	Bronchitis.
Asthma	.....	M.	49	153	90	26	.....	Arterio-sclerosis, hay fever.
Acute nephritis	20, 15	M.	9	135	80			
Cancer, pancreas	.....	M.	40	125	80	20	$98^{3}/_{5}$	Jaundice marked.
Malaria	454	M.	21	100	80	20	$98^{2}/_{5}$	Between paroxysms.
"	770	...	24	95	...	...	.....	" "
"	P. P.	M.	34	100	64	...	$96^{3}/_{5}$	" "
"	T.	M.	37	150	132	...	102	During chill.
"	T. de B.	M.	19	125	76			
"	V. P.	M.	37	118	98	...	100	
"	19, 46	M.	41	138	92			
"	19, 45	M.	25	105	72			
"	19, 47	M.	49	105	86			
"	454	M.	21	100	80	20	$97^{3}/_{5}$	Between paroxysms.
	468	M.	19	130	70	20	98	" "
Rheumatic fever	B. K.	F.	18	110	88			
" "	B. K.	F.	13	118				
" "	465	M.	24	140	120	24	103	Rheumatic fever, erythema multiforme.
" "	376	M.	36	150	80	20	99	Rheumatism.
" "	21, 89	M.	16	115	60	24	99	
Fracture of skull	M. B.	M.	43	145	92	20	$97^{4}/_{5}$	Fracture of vault; no symptoms.
Chronic rheumatism	516	M.	28	125	70	20	97	

Some remarks upon the foregoing miscellaneous cases are, perhaps, not out of place. It will be noticed that two cases of catarrhal jaundice were accompanied by hypotension.

But little information was obtained from cases of malaria. Repeated observations were made upon the same individual before, during, and after the chill, without any definite relations being established; the tension varied but little despite the wide fluctuations of temperature.

The same may be said of rheumatic fever, and tends to corroborate Mosen's[13] statement that blood pressure bears no constant relation to temperature.

Cases of Individual Interest.

Case I.—J. J., a male negro, aged thirty-six years, had been treated in the ward for some time for aortic and mitral insufficiency complicated with parenchymatous nephritis. One morning he was found semiconscious, and it was immediately noticed that the man had a right-sided hemiplegia, with Cheyne-Stokes respiration. Before the onset of the paralysis the blood pressure had ranged from 130 to 150, the patient usually feeling better when it was high. While the Cheyne-Stokes syndrome persisted there was invariably a considerably (10 mm. to 25 mm.) higher tension during the dyspnœic than during the apnœic periods.

					Cheyne-Stokes resp.					
150	130	142	142	142	A. 155	138	135	145	128	122
					D. 180	155	150			

Case II.—A man, aged fifty-two years, suffering from parenchymatous nephritis, moderate atheroma, and Cheyne-Stokes respiration, showed tension of 155 during dyspnœic and 140 during apnœic periods,

Numerous similar cases have been reported.

Case III.—P. B., male, aged forty-six years, aneurism of the aorta was diagnosed; the patient improved and left the hospital.

Right radial . . .	144	156	150	150	140	132	131	130
Left radial	134	146	140	140	130	122	121	122

Case IV.—A female, aged fifty-seven years, marked atheroma, chronic interstitial nephritis; right-sided hemiplegia. On several successive days the blood pressure in the right arm was 285 mm., while that in the left was 245 mm. Pulse 80.

A similar case in a man, aged forty-four years, who also had right-sided hemiplegia. Pressure in the right arm 146 mm.; in the left 136 mm.

Case V.—Jennie B., aged thirty years, pleural effusion. Pressure, 110 mm. Two days after aspiration of fluid 98 mm.

Case VI.—Helen K., aged forty years, atrophic hepatic cirrhosis, with ascites. Pressure, 153 mm. After paracentesis abdominalis, 148 mm. A few hours before death 109 mm.

Case VII.—William J., aged forty-five years, interstitial nephritis. Pressure, 185 mm. After hot pack, temperature 170 mm.

In the present state of our knowledge the height of the blood pressure cannot be said to be a useful index in regard to the potency of the systemic circulation, nor is it a criterion of sufficient constancy to be used as a basis for prognosis. The pressure index may, in some instances, be regarded as a relative indication for treatment. What, as a rule, we require to know is not so much the actual height of tension as the amount and character of its fluctuation. We have seen that a fair state of nutrition may be carried on in the convalescence from typhoid fever with a tension of 85 mm., and in arterio-sclerosis at 180 mm.

In conclusion, I wish to acknowledge my indebtedness to the late Dr. Frederick A. Packard, at whose suggestion I undertook the foregoing investigations, and whose noble example I shall always cherish in memory as the type of what is highest and best in the medical profession. A doctrine which Dr. Packard always sought to inculcate in the minds of the younger men was: that it is the duty of every practitioner to contribute his share, however small, to the advancement of medical knowledge; and it is with the hope of its proving of some value in the ultimate solution of the great problem of hæmodynamics that this short study has been brought to publication.

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REVIEWS.

MATERIA MEDICA, THERAPEUTICS, MEDICAL PHARMACY, PRESCRIPTION-WRITING, AND MEDICAL LATIN. By WILLIAM SCHLEIF, Ph.G., M.D. Second edition, revised and enlarged. Philadelphia and New York: Lea Brothers & Co.

THE author has succeeded in condensing an astonishing amount of information in the comparatively small compass of this book. It is for the student's benefit, no doubt, that many remedies now of purely historical interest have been retained. We note the statement that veratrum viride is given in the early stages of pneumonia, a myth that has been taught and will, we doubt not, continue to be taught to generations of confiding students; yet who ever heard of its being actually used in practice? But if the author may be criticised for excessive conservatism in this respect, he has at least omitted none of the important newer remedies, and, except for the very newest, which are found in a special list and are briefly and impartially mentioned with little or no critical comment, have been, with excellent judgment, included in the same group with the old-established drugs. It is to be regretted that the group of coal-tar antipyretics has been accorded such favorable notice. Antipyrin, it is true, is encumbered with a caution as to the possibility of medicinal doses causing "serious depression;" nevertheless, it is distinctly recommended in typhoid and pneumonia "whenever it is evident that the elevation of temperature of itself is harming the patient." Not to dwell on the difficulty of determining when this indication is present, it is now generally held, and ought to be as generally taught, that these drugs have no place in the treatment of continued fevers, especially typhoid, as there are equally effectual means of combating fever that are free from the depressing qualities of coal-tar derivatives. The antitoxins, except that of diphtheria, are dismissed with only a casual mention. The value of diphtheria antitoxin is, of course, distinctly recognized, and accurate dosage, according to age, is given. This, as well as the treatment of animal gland extracts, of which thyroid extract and the suprarenal gland preparations are favorably mentioned, represents the present status of the question of serum and animal therapy, and is in accord with general clinical experience.

In the portion of the book devoted to prescription-writing, the claims of the metric system to be admitted to general practice are fully recognized, and we cordially join with the author in the hope that the adoption of the system by the Pharmacopœia may lead to its adoption by the profession generally. As long as we continue to think in the old system, some method of transposition will be indispensable, and the one suggested by the author is as convenient as any. In writing ordinary prescriptions, which do not demand absolute accuracy of dosage, it will save time and trouble to bear in mind that the number of teaspoonful doses

in a 2-ounce mixture is equal to the number of grains—approximately 16—in a gramme; it is, therefore, only necessary to write opposite the name of the ingredient the number representing the desired dose in grains or minims, since it will represent the number of grammes or cubic centimetres required for the whole mixture. If the mixture is to be three ounces—100 cubic centimetres—the numbers are multiplied by 1½; if the dose is to be two teaspoonfuls, the numbers are divided by 2, etc., according to the amount of the mixture and of the dose desired. For drugs that are prescribed in fractional doses, the equation 1 grain equals 0.06 gramme must be carried in the mind.

The short abstract of dietetics, which should properly be regarded as an integral part of therapeutics, is a valuable addition to the book. A table of doses, a list of the important poisons and their antidotes, with other tabular matter, and two complete indices, one "general" and one "therapeutical," complete the volume, which, as regards arrangement, type, and other details relating to book-making, is a good example of the up-to-date text-book. R. M. G.

A Compend of Human Physiology. By Albert P. Brubaker, M.D. Eleventh edition. Philadelphia: P. Blakiston's Son & Co.

Another edition, the eleventh, bears witness to the popularity of this quiz-compend of physiology, which is too well known to the student world to require a formal introduction. It is not compiled on the question and answer plan, and therefore discourages the objectionable plan of learning by heart, which is the immediate result of using many of the so-called aids to students. The book is cordially recommended to students for whom it is intended, and it will no doubt be consulted by older men as well in looking up a question of physiology after the store of college information has grown rusty. The text is diversified with some excellent illustrations and numerous tables. The index is not much more than nominal, and were it not for the excellent arrangement of the subject-matter and the abundance of headings that catch the eye one might be disposed to grumble at the author's parsimony in that respect. R. M. G.

A Text-book of Surgical Principles and Surgical Diseases of the Face, Mouth, and Jaws, for Dental Students. By H. Horace Grant, A.M., M.D., Professor of Surgery and of Clinical Surgery in Hospital College of Medicine; Professor of Oral Surgery in the Louisville College of Dentistry, etc. Philadelphia and London: W. B. Saunders & Co., 1902.

It is of prime importance that a dentist should understand something of the principles underlying general surgical practice and that he be able to properly interpret the initial symptoms of certain conditions which may first come to his notice. We refer to such diseases as chancre, cancer of the tongue, cancrum oris, fibroid growths of the jaws, etc.

And, again, this knowledge must be called into play in the treatment of those conditions where the general surgeon and the dentist are associated. The book before us is written by a general surgeon for the instruction of dental students. It presents in simple language exactly what a dentist should know about surgery in general, such as inflammation and its results, anæsthesia, hemorrhage, tumors, etc. The presentation of these subjects is much after the style of that found in the smaller works on general surgery.

One criticism we have to offer is that the discussion of cleft palate occupies but three pages and is illustrated by only three cuts. This would certainly seem to be a surgical condition about which dentists should be well informed. Much has lately been written upon the treatment of cleft palate, particularly by the English surgeons, and yet little reference is made to what has been accomplished by the recent methods of treatment. The illustrations of the book are especially good. We regret to see that under the head of neuralgia the author has not warned the dental student against the removal of teeth for the relief of trifacial neuralgia. We feel that such advice is necessary, since so frequently cases of tic douloureux involving the second and third divisions of the nerve come to the surgeon with a number of all the teeth on the affected side extracted. Dentists should be made to understand that the extraction of teeth never relieves the condition, although the pain may be referred to them. J. H. G.

A Manual of Medical Treatment or Clinical Therapeutics. By J. Burney Yeo., M.D. Chicago: W. T. Keener & Co., 1902.

The tenth edition of this work is issued in two conveniently sized volumes, comprising more than fourteen hundred pages. The material is arranged in an interesting and thoroughly practical way. Wherever it has been possible in the consideration of a disease, the mode of causation, the morbid changes, and the probable manner in which the remedial agencies influence its course have been set forth. Thus the reader is enabled not only to learn the treatment of diseased conditions, but also to get a fairly comprehensive grasp of other important facts found usually only in books on practice. The work will be found satisfactory. T. A. C.

A Text-book of Pathology and Pathological Anatomy. By Dr. Hans Schmaus. Translated from the sixth German edition by A. E. Thayer, M.D., and edited with additions by James Ewing, M.D. Illustrated with 351 engravings, including 35 colored insert plates. Philadelphia and New York: Lea Brothers & Co., 1902.

Dr. Ewing in his edition of Dr. Schmaus' text-book of *Pathology* has contrived to arrange a book adapted especially for the need of students. It is by no means a book of reference, and all discussions and bibliography are carefully omitted. Indeed, the total lack of

quotation of authorities is noticeable, and seems not altogether satisfactory. The book is divided into two parts, the first dealing with general pathology, in which are included chapters on disorders of circulation and regressive and progressive processes; while the second part is devoted to the subject of special pathology, in which the various systems of organs are treated in order. The fundamental principles of inflammation, tissue repair, and regressive changes are fully described, and the subject of tumors is well dealt with. A very short account is given of the more important parasites. In the special pathology the main changes affecting the different organs are recounted, and frequently clinical data are also added. The details of histological change are often subordinated to a general survey of the disease, and no attempt is made to set forth the nicer problems of cellular pathology or to introduce the results of researches so recent that they would necessitate discussions. The diseases of the nervous system are treated of quite fully and adequately. Numerous illustrations are used to elucidate the text.

W. T. L.

A Manual of Materia Medica and Pharmacology. By David M. R. Culbreth, Ph.G., M.D., Professor of Botany, Materia Medica, and Pharmacognosy in the Maryland College of Pharmacy; Professor of Materia Medica and Pharmacognosy in the University of Maryland Medical and Dental Schools. Third edition, enlarged and thoroughly revised. Pp. 916. Philadelphia and New York: Lea Brothers & Co., 1903.

The third edition of this work comes to us offering ample evidence of enlargement and thorough revision, to be found in each portion of the book. The author's desire for increased accuracy in the old and intelligent discrimination in the selection of materials for the new has reached satisfaction. While the previous editions were worthy of and received commendation, the present must command more; the author, incited by the success already attained, has renewed his efforts, and the result is especially satisfactory. The first fifty pages are devoted to definitions, forms of medicines, avenues by which they are introduced into and means by which they are transmitted through the system, and the conditions which may modify the action of remedies. The various methods by which medicines may be classified are presented, and the author announces his—that by natural affinities; beginning with the lowest and proceeding to the more highly developed, drugs are grouped together as (1) organic, from the vegetable kingdom; (2) from the animal kingdom; (3) inorganic, from the mineral kingdom; (4) organic carbon compounds; (5) non-pharmacopœial organic carbon compounds. This portion of the work is well and thoroughly done, and in its scope is a full presentation of materia medica. The pharmacology as found in "Properties" and "Uses" is brief and quite sufficient for the student of pharmacy, but the student of medicine will probably regard it as rather a guide to more extensive and necessary works on pharmacology and therapeutics.

Part VI. covers twenty pages devoted to the microscope and its use in materia medica. In the Appendix we find an excellent section devoted to Poisons—Treatment and Antidotes. Of Prescription Writing by the

Physician this may be said—complete presentation demands more space and thoroughness of development than is found here. The miscellaneous tables of weights, measures, doses, drops, thermometers, abbreviations, constituents, pronunciations, are all useful, and, as such, important. We wish, however, that on page 870 the author had stated the capacity of domestic measures as they are more commonly met with rather than those commonly accepted. Amid such general excellence of diction a few expressions become disagreeably noticeable; for example, "*gulp*" (p. 21), and "*children are very acute to opium*" (p. 26). For a systematic treatise upon the materials used in the treatment of disease, to which is added a brief exposition of their properties and uses, the student of pharmacy may turn to Culbreth resting assured that the information which he will obtain will be full and accurate. We congratulate the author upon the completion of his third edition, and feel that this is but the forerunner of many succeeding revisions. R. W. W.

Atlas and Epitome of Diseases of the Mouth, Pharynx, and Nose. By Dr. L. Grunwald, of Munich. Second edition, revised and enlarged. Authorized Translation from the German. Edited with additions by James E. Newcomb, M.D. Containing 102 illustrations on 42 lithographic plates, and 41 figures in the text. Philadelphia and London: W. B. Saunders & Co., 1903.

The uniform excellence of this series of hand atlases is not marred by this number of the series. In former days plates such as those contained within it would have only been got out by the publishers in huge, unwieldy volumes. In this little work all the essential parts of the large plates are produced, and the various illustrations are chosen with so much judgment that the book may be regarded as constituting a complete pictorial guide to diseases of the upper respiratory tract. Under the able editorship of Dr. Newcomb the text of this volume is especially good. He has incorporated some additions which add greatly to the value of the German text; thus, he describes the form of tonsillitis occasioned by the bacillus of Vincent, and also Koplik's spots. The book constitutes an invaluable companion for the specialist and a most reliable guide for the student and practitioner. F. R. P.

Anatomy and Histology of the Mouth and Teeth. By I. N. Brownell, M.D. Second edition, revised and enlarged. Philadelphia: P. Blakiston's Son & Co., 1902.

The first edition of Dr. Brownell's book had already won for itself a gratifying position as a most excellent manual of the subjects which it purported to teach. The present edition has given him the opportunity to revise the few small errors which invariably happen in the first appearance of any book, and also to add material of much value to the work. An excellent addition has been made in the chapters pertaining to the embryology of the mouth and anomalies of teeth formation and

structure. The illustrations are numerous and excellent, and the volume is one of the most up-to-date text-books upon the subject of the anatomy of the mouth which has appeared in recent years. D. S. R.

Die Protozoen als Parasiten und Krankheitserreger. Presented from a biological standpoint. By Dr. F. Doflein. Pp. 274, with 220 illustrations. Jena: G. Fischer, 1901.

It is seldom one sees a text-book of this nature in which it is so easy to find just what he wants. The arranging and indexing is perfect. After a brief but comprehensive introduction on protozoa and parasites, the author takes up the protozoan parasites systematically and in detail. The descriptions, though at a time sketchy, are much helped out by the copious illustrations. Some of the illustrations are original—more, however, after the original drawings by those who have given the first descriptions of the organism. In the case of each organism, particular attention is given to its life cycle and the various hosts invaded by it; and, further, there is added a brief statement of lesions and symptoms produced in the host. The text is completed by reference to the original description of such species, a section on technique for each important group, and a bibliography for each class, indicating the more important works on the subject. The book is completed by a table of contents, index of subject-matter, of hosts, of authors, and of illustrations. Though one may not agree with the author as to proper terminology and as to some minor points of interpretation, the book as a whole is one to be recommended to those interested in the parasitic diseases of protozoan origin. C. H. B.

Progressive Medicine. Vol. III., September, 1902. A Quarterly Digest of Advances, Discoveries, and Improvements in the Medical and Surgical Sciences. Edited by Hobart Amory Hare, M.D., Professor of Therapeutics and Materia Medica in the Jefferson Medical College of Philadelphia. Octavo, cloth, 421 pages, 26 illustrations. Philadelphia and New York: Lea Brothers & Co.

In close accord with the high standard of excellence set by preceding numbers, there has appeared the third volume of *Progressive Medicine* of this year. The first part, by W. Ewart, deals with the Diseases of the Thorax and Its Viscera, including the heart, lungs, and blood-vessels; the second, by W. S. Gottheil, with Dermatology and Syphilis; the third, by W. G. Spiller, with the Nervous System; the fourth and last, by R. C. Norris, with Obstetrics. Each of these articles, in addition to containing a résumé of the more important of the recent work upon its respective subjects, is enhanced in value by the embodiment of the notes and comments of the able contributors, whose eminence in their particular branches entitles their opinions to consideration and respect.

The choice of the articles abstracted, as well as the terse and lucid manner in which they are set forth, renders the book of invaluable

service to the practitioner who tries to keep abreast of the vast and voluminous wave of modern medical literature. G. W. N.

THE PRACTICAL MEDICINE SERIES OF YEAR BOOKS. Under the general editorial charge of GUSTAVUS P. HEAD, M.D. Vol. X. Skin and Venereal Diseases; Nervous and Mental Diseases. Edited by W. L. BAUM and HUGH T. PATRICK. Chicago: The Year Book Publishers.

THE rapid growth of knowledge in every department of medicine provides such abundant material for year books and similar publications that the editors of this volume deserve the reader's thanks for keeping it within such moderate limits. The selection of the material attests their excellent judgment as well as their diligence, and while the treatment of the various subjects is necessarily brief, the book is most suggestive, and the abundant bibliographical references incite to further study. Although the book is so compact and the subject-matter judiciously arranged under bold-faced headings, a very full index is also added, which makes the finding of any desired subject the work of only a few minutes. R. M. G.

REGIONAL MINOR SURGERY, DESCRIBING THE TREATMENT OF THOSE CONDITIONS DAILY ENCOUNTERED BY THE GENERAL PRACTITIONER. By GEORGE GRAY VAN SCHAICK, M.D., Attending Surgeon to the French Hospital, New York. New York: The International Journal of Surgery Company.

IT has been the author's aim to present a small book which might act as a guide to the general practitioner in treating certain minor ailments and injuries of a surgical nature. This, we think, he has well done. The opening chapter deals with asepsis, and the reader is impressed with its importance even in the performance of the most trivial surgical operation. The suturing of wounds is carefully described, and an excellent little diagram, which we have never before seen, is given, showing the method of closing a semicircular wound. This is the sort of book which it would be well for every new graduate, whether he is going at once into practice or whether he is to become a hospital resident, to read, as he will find here many minor practical points which the larger text-books do not present.

There are a number of subjects which one might suppose the author would have included in a book of this kind, but, on the whole, we think he has made a wise selection. One omission, however, we can but call attention to, and that is the absence of any chapter dealing with the treatment of fractures of the upper extremity. These fractures are very frequently treated by general practitioners. Great improvements have been made in their treatment during recent years, and we feel that the addition of a chapter or two on this subject would greatly enhance the value of the book. Another criticism we would offer is the fact that the author's description and illustrations of the Gibney adhesive strip dressing for sprains of the ankle is not the Gibney dressing as we

know and practice it. Although before reading this book we would have doubted the desirability of such a work, we now realize the want of it and commend the present volume. J. H. G.

A Manual of Dissection and Practical Anatomy. Founded on Gray and Gerrish. By William T. Eckley, M.D., Professor of Anatomy in the Medical and Dental Department of the University of Illinois, the Chicago School of Anatomy and Physiology, the Chicago Clinical School, and West Side Training School for Nurses, and Corinne B. Eckley, Demonstrator of Anatomy in the Medical and Dental Departments of the University of Illinois and Chicago School of Anatomy and Physiology, and Member of the American Association of Anatomists. Illustrated with 220 engravings, 116 of which are colored. Philadelphia and New York: Lea Brothers & Co., 1903.

The fact that a new manual of dissection has been offered by the publishers would seem to indicate that there is a need for such a work. The old Dublin *Dissector*, which was so popular with our preceptors, and Heath's *Practical Anatomy*, which was the companion of our student days, will have to give way for the more modern works to be used in the dissecting-room. As announced in the preface, the present work has a twofold purpose, namely, to provide the student with a detailed guide for dissection and to answer the requirements of the physician and the surgeon wishing to review the anatomy of any region. It is prepared for practical use with either *Gray* or *Gerrish*, and a large series of illustrations have been taken from these works and placed at the disposal of the author, thereby greatly enhancing the value of the book. In addition to the usual descriptive matter found in dissectors, the work abounds in tables, and we find, in addition to the usual tables met with, it combines tables of the muscles of expression, tables of the muscles of mastication, and even tables of the branches of the vagus and tables of the cutaneous veins.

The introduction of the new nomenclature into this work has been done judiciously, but the section on metamerism would seem to be out of place in a dissector. The divisions of the abdomen as given in the abdominal topography are after the plan of Gerrish, the upper line being drawn between the tenth costal cartilages instead of between the extremities of the ninth ribs; and while the description gives the line as drawn from the highest level of the iliac crest, the illustration gives it as drawn from the anterior superior iliac spines.

The illustrations are particularly good, and can be used not only as a supplement to the text, but in many cases—as those relative to the brain—they may be used in substitution for the text in making dissections.

The table on the vascular system is greatly enhanced in value by the addition of small outline drawings incorporated into the text.

The work will be found very useful in the dissecting-room, and will also prove valuable to practitioners desiring to rehearse regional anatomy. The publishers of the book are to be complimented upon the very attractive appearance of the volume. J. K. Y.

PROGRESS

OF

MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF

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Acute Nephritis following Mumps.—PAGANELLI (*Riv. Crit. d. Clin. Med.*, 1902, vol. iii., 726), from Silvestrini's clinic, reports a case of mumps in a boy, aged nine years, who had never suffered from any of the exanthemata. At first the symptoms were light, the affection being limited to the right side, while at the same time a younger brother had bilateral parotitis. Two days later the patient became very ill: respirations, 44; temperature, 39.4° C; pulse, 120. Slight œdema of the eyelids and of the extremities, especially of the hands and feet. Urine scanty, 0.4 per cent. albumin; in the sediment, numerous hyaline and epithelial casts and a moderate number of red and white blood corpuscles. Stained specimens from urine passed into a sterile vessel showed a moderate number of bacteria, a few bacilli coloring with Gram, but no cocci which held their color with Gram. Cultures showed only a few ordinary bacteria (mesentericus, proteus, sarcinæ, and bacilli of the colon group). One rabbit inoculated with the sediment of the urine died after fifteen days of infection with a variety of the bacillus coli, while the other died after a month, of coccidiosis. After sixteen days the fever fell to normal, the œdema disappeared, the urine cleared up, and the patient rapidly recovered. The relation of this attack to the parotitis, together with the absence of evidence of any other general infection, led the author to believe that the renal process was due to the specific cause of parotitis. While slight albuminuria is not infrequent during the course of parotitis, actual acute nephritis is so unusual as to justify mention of the case.

On the Working Capacity of the Heart.—GALLI (*Münchener med. Wochenschrift*, 1902, Band xlix., pp. 953, 1005, 1049). While the recognition of weakness of the heart muscle is easy enough when recogniz-

able dilatation and subjective symptoms of dyspnœa, etc., have developed, yet it must be said that we have up to the present time possessed no satisfactory means of estimating the muscular capability of the apparently normal heart. Galli in a careful study seeks to show that valuable information concerning this important point may be obtained from a study of the reduplications of the heart sounds, and more particularly of the reduplication of the second sound heard in the pulmonic area. The majority of observers have divided the reduplications of the second sound into the physiological and pathological, regarding as physiological reduplications those occurring in apparently normal individuals which are inconstant and vary with different phases of the respiratory act. The truth of Potain's observation that the so-called physiological reduplication of the second sound is especially marked at the end of inspiration and at the beginning of expiration has been recognized by most observers. Observations as to the frequency of the reduplication, however, have varied greatly. Gerhardt found it 18 times out of 260 individuals, who were, however, for the most part patients, though the majority were not in bed; Potain, 38 times out of 500; while Landgraf in 594 healthy soldiers failed to find a single reduplication. Galli examined carefully 300 individuals—200 apparently healthy individuals, 100 others—patients in the hospital. These were examined frequently at different times of the day and under varying conditions. He made frequent examinations of 120 carabinieri at one of the barracks in Rome. His observations here were most interesting in that he found early in the morning an average of 19 reduplications in every 100 men. In the middle of the day after exercise there were 40; at half-past three in the afternoon 56. Where a reduplication had occurred in the morning it was *never* absent in the afternoon or evening. Reduplication was more frequent in the recumbent posture, in which he examined all his patients; while Landgraf's statistics were based upon examinations made in the erect posture. This he believes may be due to the fact that the left ventricle has more work to do in the erect posture, on account of the increased blood pressure which results in a slight retardation of the second aortic sound—enough to prevent a reduplication from delay in pulmonic closure. The reduplication was constantly found during recovery from infectious diseases.

What conclusions may be drawn from these observations? Dehio, while accepting the division into physiological and pathological reduplications, has stated that, in his opinion, the reduplication of the second sound when present in otherwise healthy individuals is suggestive of weakness of the right heart. Galli inclines strongly to the same opinion, believing, moreover, that the "diastolic reduplication is a valuable symptom of exhaustion of the heart muscle, and gives us, therefore, a measure of the functional capacity of the heart." The right ventricle may be called the *locus minoris resistentiæ* of the heart, and the period of the respiratory act at which this phenomenon is especially perceptible is just that time at which the greatest work is called for. "The right ventricle is . . . during inspiration, but especially at the end of inspiration, much filled with blood, and must, as a result, contract with greater energy in order to empty its contents into the pulmonary vessels—all the more since the elastic pull of the lungs reaches its highest degree at the end of inspiration;" though

it is possible that this is compensated for to a considerable extent by the simultaneous dilatation of the pulmonary vessels. If, however, the right heart be weakened, systole at the end of inspiration will be more difficult, slower, and may well result in a slight delay in the closure of the valves; and the degree of interference with the right heart will depend upon the depth of the inspirations. In cases, then, of very slight weakening of the heart muscle, the pulmonary reduplication may be heard only at the end of inspiration—"a reduplication of the first degree." If the weakness be a little more, the difficulties in the way of contraction of the ventricle may last for a few beats into expiration —"a reduplication of the second degree." Where severe alterations of the cardiac muscle are present we may have a persistent reduplication during all phases of the respiration —a "reduplication of the third degree." Delay in the second aortic sound may also occur, but for different reasons, which the author considers.

According to Galli, then, diastolic reduplication is a symptom of exhaustion of the heart muscle, which may depend upon four causes: (1) Diseases of the heart muscle; (2) elevation of pressure in the pulmonary vessels or the aorta; (3) modifications in the pull exercised by the lungs ("Lungenzug"); (4) nervous causes. The recognition of these facts is a matter of importance because of the value of rest and proper treatment in early cases. His conclusions are as follows:

1. The present division of reduplications into physiological and pathological is not justified, since it does not rest upon clinical facts; they should rather be divided into reduplications of the first, second, and third degree.

2. Diastolic reduplication is always and under all circumstances a pathological phenomenon; that of the third degree is the worst and the least influenced by the rest.

3. Diastolic reduplication is an indication of insufficiency of the heart, and is therefore a good criterion for the estimation of the functional capacity of the heart.

4. It is necessary to separate the pathology of the heart sharply into that of each side, and to distinguish between reduplications due to affections of the right and of the left ventricle.

5. Rest is the best method of treatment for diastolic reduplications and the best method to prevent the development of cardiac insufficiency.

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1. Experiments on the Effects of Freezing and Other Low Temperatures upon the Viability of the Bacillus of Typhoid Fever, with Considerations Regarding Ice as a Vehicle of Infectious Disease. 2. Statistical Studies on the Seasonal Prevalence of Typhoid Fever in Various Countries and its Relation to Seasonal Temperature.—Sedgwick and Winslow (*Memoirs of the American Academy of Arts and Sciences*, vol. xii., No. 5, pp. 472–577) conducted a series of very elaborate experiments on the effects of freezing and other low temperatures on the typhoid bacillus, with the view of determining the degree of risk of typhoid fever being contracted from infected ice. They also endeavor to find an explanation for the autumnal prevalence of typhoid fever by a most elaborate statistical study of the disease in various countries.

The authors first give an exhaustive review of the literature relating to ice

as a vehicle of disease, and to the bacteriology of ice. The work that has been done along this line leads them to the conclusion that about 90 per cent. of ordinary water bacteria are eliminated by the process of freezing. They found that the work that had been done on the percentage reduction of the specific pathogenes, and in particular of the typhoid bacillus, the most important one, was very meagre. The only experiments that dwelt quantitatively with the effect of cold on this organism were four in number: three by Prudden, and one by the biologists of the Massachusetts State Board of Health. They considered this to be meagre evidence on which to base conclusions as to the importance of ice supply as a possible source of typhoid fever, and proceeded to supplement this evidence by a careful series of bacteriological studies.

It is impossible to give here even a brief account of how these were carried out. It suffices to say that they were most painstaking and thorough. They found that about 50 per cent. of the typhoid bacilli were killed during the first half-hour of freezing. Less than 1 per cent. of typhoid germs in water survive fourteen days of freezing. Thawing and refreezing are somewhat more fatal than simple freezing. Four successive freezings and thawings do not, however, suffice to kill off the most resistant bacilli. Typhoid bacilli behave in water just above the freezing point much as they do in ice. A large proportion are killed by a few minutes' exposure. In the next few hours the reduction proceeds *pari passu* with the duration, while a few germs persist for some time. Ice formed on the surface of a quiet body of water contains only about 10 per cent. of the bacteria contained in the water just below. This difference is believed to be due to physical exclusion by the process of crystallization and not to any germicidal action.

From these results and from other evidence the writers bring forward they conclude that the risk of contracting typhoid from the use of natural ice is infinitesimally small. The risk is greater, however, with artificial ice if the water is not perfectly pure. Epidemiology has clearly shown that disease follows best a direct, quick transfer of infectious material from patient to susceptible victim; and inasmuch as artificial ice is used quickly after its manufacture, the possibility of purification by time is excluded, and such ice might therefore be a menace to public health.

Although certain writers have claimed that typhoid is not more frequent at any particular season of the year, yet the concensus of opinion is strongly in support of the view that typhoid fever the world over is much more frequent during the fall months. While in this latitude these months are September, October, and November, they are not the same everywhere, the seasons varying according to longitude and certain physical conditions.

Sedgwick and Winslow proceed to find some explanation for the autumnal prevalence of typhoid fever. After an exhaustive review of the literature on the subject they come to the conclusion that none of the explanations advanced, including the ground-water theory of Pettenkofer and the Munich School, adequately account for this seasonal relationship. They give credit to Murchison, Liebermeister, Davidson, and Woodhead for having pointed out an association between the high temperatures of summer and the prevalence of typhoid in the fall. The reason for this had never been explained, and their views never gained general acceptance.

The writers thought that their bacteriological work on the effect of low temperatures upon the typhoid bacillus supported the idea that the temperature really might in itself exercise a direct effect upon the etiology of the disease. They hoped to be able to prove this by the study of statistics gathered from a wide field. Accordingly they brought together statistics of the monthly variations in temperature and in the prevalence of typhoid fever for thirty large cities or communities scattered over the whole world. Four continents and both hemispheres were represented. The temperature and typhoid statistics were tabulated for each place for a number of years—usually ten. They plotted curves representing the mean monthly temperatures and typhoid cases or deaths for these periods for each community. In twenty-one of the communities the curves were almost identical, the only difference being that the apex of the temperature curve was at its height just two months before that of the typhoid curve, so that by shifting the typhoid curve just two months ahead the two curves were found to be practically identical. The temperature curve was highest about August 1st, and the typhoid curve highest about two months later. The failure of the curve to present itself in the nine other communities was explained by the investigators by local conditions, so that in their opinion these instances did not diminish the importance of the evidence in the twenty-one districts.

The writers think that the increase of typhoid fever with a gradual rise in the mean air temperature of a given locality is a phenomenon so widespread that it indicates beyond reasonable doubt some relation between the two factors.

Of the three great intermediaries of typhoid transmission—fingers, food, and flies—they hold the last to be the most important. The relation of this factor to the season is close and complete, and they claim that a certain amount of the autumnal excess of typhoid is undoubtedly traceable to the presence of large numbers of flies. They hold, however, that none of the usual factors cited, including the activity of flies and the exposure of urban subjects to rural unsanitary conditions, can explain the autumnal prevalence of typhoid and its close relationship with high summer temperatures. They believe that their experiments lead them to reasonably suppose that it must be more difficult for the typhoid organism habituated to a temperature of 98° F. to persist in nature when the thermometer is at 30° than when it is in the neighborhood of 80°. They assert that it is the absence of the destructive influence of cold rather than any stimulating influence of heat which permits the rise culminating in the autumnal maximum.

The typhoid organisms are carried over the winter in the bodies of a few patients, or possibly in vaults, or in other deposits of organic matter, where they are protected from the severities of the winter. The number of persons who contract the disease from these winter cases will depend upon the length of time that the organisms remain alive and virulent. The length of the period during which the microbes live will depend largely on the general temperature. As the season grows milder, more and more of each crop of germs sent at random into the outer world will survive long enough to gain entry into a human being. The process will be cumulative. Each case will cause more secondary cases; and each of the latter will have a still more extensive opportunity for causing infection. The warm temperature of the

late summer favors the development of the organism, causing more numerous infections, which manifest themselves in the fall. As winter approaches the organism finds less favorable temperature environment, and the cases gradually diminish again.

THERAPEUTICS

UNDER THE CHARGE OF

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A New System of Treating Pulmonary Phthisis.—DR. DUNCAN TURNER speaks of the improvement taking place on the old line of treating patients in sanatoria when he introduced the use of electricity (cataphoresis), massage and the rubbing of cod-liver oil. The oil-massage is made daily. The patient, after being hardened by repeated cold sponging for two or three days, lies on a couch naked. His body is then sponged with a weak solution of sodium bicarbonate, one drachm to the pint. The oil mixture is then rubbed in all over the trunk from the neck to the pelvis, back and front, the quantity used at one time being from one to two tablespoonfuls. It should be rubbed in vigorously. When galvanism is used generally one pole is applied over the solar plexus and the other is moved up and down over the upper part of the spine.—*The Lancet*, 1902, No. 4129, p. 1047.

Methylene Blue and Quinine in Malaria.—DRS. JOHN T. MOORE and W. L. ALLISON made an extensive series of studies on these two drugs in their effect in the malarial organism. They conclude that: 1. Methylene blue is probably most valuable in chronic cases, but has no advantage over quinine. 2. Methylene blue will destroy malarial parasites in many cases, but is less certain than quinine. 3. The effects of methylene blue are ordinarily more unpleasant than quinine. 4. It is useful for patients who cannot take quinine on account of some idiosyncrasy to it. Its use in cases of pregnancy is undetermined. 5. It is probably valuable in treating hæmaturic and hæmoglobinuric fevers on account of its diuretic action; this has yet to be determined. They had no opportunity to test its use in such cases. 6. They believe that quinine is quicker and much more certain, and would rely upon it rather than upon methylene blue.—*Medical News*, 1902, vol. lxxxi. p. 1063.

Pure Urea and Pulmonary Tuberculosis.—DR. VERE PEARSON reports on his experiments with pure synthetized urea in the treatment of pulmonary tuberculosis, and basing his results upon a comparison of the progress made

by his patients, with the average progress made by similar patients in the Brompton Hospital, he shows that of 100 patients over twelve years of age —75 males, 25 females—nine died, seventeen lost weight, seven remained stationary, and the rest gained in weight from one and one-half pounds to twenty-three pounds. Among those who gained in weight the majority showed improvement in physical signs as well as in general condition. In the great majority the temperature and the pulse improved as well, and the expectoration diminished. Urea seemed to exert no special influence upon either the pulse or the temperature, and in no case was there any marked diminution in the quantity, or any appreciable improvement in the quality of the sputum. The conclusions arrived at, the author says, do not, of course, exclude the possibility that urea acts beneficially in cases of tuberculosis other than pulmonary, such, for example, as glandular tuberculosis and lupus, but so far as it was possible for him to judge from the results obtained in his cases he does not believe that there is any special action exerted by pure urea.—*The Lancet*, 1902, No. 4134, p. 1383.

Sodium and Potassium Iodides and Their Clinical Use.—Dr. R. B. Wild gives an elaborate study of the comparative value of these iodides. Clinically potassium iodide is claimed to be more active, but is also more liable to cause iodism. He discusses in great detail three factors that are concerned in the action of these iodides: 1. The salt action. 2. The "ion" action of dissociation of the molecule into two moieties which become charged with negative and positive electricity. 3. The supposition that the alkaline iodides are decomposed in the tissues, setting free nascent iodine. Apart from theoretical consideration, the author thinks that the potassium salt is to be preferred, owing to its extreme solubility and rapid diffusive power favoring its penetration to all tissues. Its power of dilating bloodvessels is of great importance, by bringing more blood to the tissues, thus stimulating nutrition and bringing more of the drug to the tissues. As regards two common objections, namely, the liability to iodism and the depressing effect of the potassium, Wild holds that there is little difference between the sodium and the potassium in small doses, but the vascular dilatation of potassium iodide may predispose to catarrhal inflammations and cutaneous eruptions. As for the depressing effects, this is much exaggerated, and to a considerable extent can be further avoided by modifying the diet so as to diminish the amount of potassium salts. Thus potatoes and legumes should be forbidden, and green vegetables are only to be taken in small quantities; but milk, fish, eggs, and the animal foods are to be freely allowed.—*Medical Chronicle*, 1902, vol. xxxvi. p. 285.

Morphine Addiction and Its Treatment.—Dr. C. B. Burr reports a series of twenty cases of this addiction, giving some very interesting and out of the ordinary deductions, the which are nearer actual conditions than many of the cut-and-dried text-book opinions. With reference to the withdrawal of morphine he favors its rapid withdrawal—*i. e.*, within a week to ten days. In some patients a shorter time even may be considered—two to three days—and thus far he has not seen any evil results from the abrupt withdrawal method, although it should be a primary canon that patients

should be handled according to their individuality rather than because of their being morphine *habitués*. In general, on admission to the sanitarium the patients receive a hot Russian bath, and following this the morphine is rapidly withdrawn, strychnine, quinine, kola, coca, champagne, and aromatic spirit of ammonia are given at night. In prescribing chloral the author advises its combination with quinine or strychnine, and at the height of the constitutional disturbance, which he finds to be, as a rule, about the third day following the withdrawal of the drug, he advises the use of $\frac{1}{4}$ to $\frac{1}{2}$ grain of morphine hypodermically; this rests the body and brings about a relief from the nervous tension and does not interfere with the progress of the treatment.—*Journal of the American Medical Association*, 1902, vol. xxxix. p. 1558.

Two New Drugs: Hopogan and Extogan.—Dr. D. M. Frenkel describes two new drugs—magnesium peroxide, called hopogan, and zinc peroxide, called extogan—both prepared in a pure state. Hopogan is a white, light, tasteless and odorless powder, almost insoluble in water. The filtered emulsion gives a liquid with a slight alkaline reaction, containing small traces of chloride of sodium. The product is composed qualitatively of magnesium and oxygen. It contains 7.15 per cent. of active oxygen, which corresponds to 25 per cent. of magnesium peroxide. Extogan is a light, slightly yellowish, tasteless, odorless powder. It is absolutely insoluble in water. It contains traces of sodium chloride. Its qualitative composition is zinc and oxygen. It contains 9.08 per cent. of active oxygen, corresponding to 55 per cent. of zinc peroxide. Although no clinical work has yet been done upon these drugs, it is believed that they will interest experimenters. Zinc peroxide (extogan), intended for internal use, contains in a latent state, so to speak, oxygenated water. The physician can convert it into its active state on the wound or diseased epidermis, and can regulate its quantitative production. To produce this oxygenated water, tartaric acid would seem to be the best agent. Three parts of zinc peroxide and four parts of tartaric acid will produce oxygenated water at 100 per cent. Clinical experience ought to show that active oxygenated water thus locally generated should have a much stronger bactericidal and cicatrizing effect than ordinary oxygenated water. Magnesium peroxide (hopogan) is intended for internal use; the maximum dose is yet to be determined clinically, but it is thought that one and one-half grammes of pure magnesium peroxide or six and one-half grammes of hopogan in the scale of 25 per cent. of peroxide would present no danger. Once in the stomach, magnesium peroxide is decomposed by the normal or abnormal gastric juice and the oxygen liberated, which, in the case of abnormal condition, probably attacks the products of butyric acid fermentation. However this may be, it must be remembered that the decomposition of magnesium peroxide in the stomach is always accomplished by an appreciable local rise of temperature. The practical value of these drugs is still to be determined by laboratory and clinical experiment. It should be mentioned that the iodides, under the action of magnesium peroxide, give forth iodine, which will make it possible as in no other way to produce iodine in the nascent stage in a quantity that can be exactly calculated in advance.—*Le Progrès Médical*, 1903, vol. xvii. p. 19.

A Study of Tuberculin.—Dr. F. M. Pottenger, in reviewing the status of knowledge concerning tuberculosis when Koch made his discovery, makes the distinction that tuberculin was claimed by Koch to be a cure in early cases of tuberculosis, not in consumption. Along this line he has made a study of tuberculin and allied products, with reference to their action and the proper method of administration. He states that the sanitarium is the ideal place for treating patients by culture products, and that the physician who would use them successfully in general practice must be not only a great, good, general practitioner, but have a thorough knowledge of the pathology, diagnosis, and clinical course of tuberculosis, and understand the proper application of the remedy. He suggests that the patient about to be treated by culture products should be under careful supervision for two days, with a two-hour temperature chart. Suitable places for giving the injection are the loose tissue between the scapulæ, over the chest, below the clavicles, and in the belly of the triceps. The effects produced depend on the amount of dosage, being slight in small doses, and showing three or four degrees of temperature in large doses. There may be weakness, aching, and nausea, and a severe local reaction. The remedies, by stimulating the tissue, cause resolution to hasten, and also produce immunity. Though chiefly of value in early stages, they benefit areas of recent extension that are purely tuberculous in advanced cases. Old tuberculin (Koch) is seldom used, but when it is the initial dose should be small, one one-hundredth to one-tenth of a milligramme. The new tuberculin T. R. (Koch) has for an initial dose one one-thousandth to one five-hundredth milligramme, injections to be repeated every day at first, doubling the preceding dose till one-tenth of a milligramme is reached. Purified tuberculin (von Ruck) has for the initial dose one-tenth of a cubic centimetre, to be increased every other day by one-tenth of a cubic centimetre until five-tenths of a cubic centimetre is given. Watery extract of tubercle bacilli (von Ruck) have the advantage over T. R. of being stable. The administration is begun by using one-tenth of a cubic centimetre and increased according to susceptibility as in the other products. A slight rise of temperature during administration is not to be disregarded. If there are infiltrations in the larynx the local reaction, which, detected upon laryngoscopic examination, serves as an excellent guide to dosage. A distinctive feature that makes the rise of temperature caused by the remedy is that the elevation stops on its withdrawal. The author finds that by using culture products in addition to the nutritious food, fresh air, rest, exercise, and hydrotherapeutic measures, 20 per cent. more patients are cured than when these remedies are admitted.—*Therapeutic Gazette*, 1903, vol. xxvii. p. 12.

Hyoscine for the Morphine Disease.—Dr. R. C. Rosenberger reports an interesting history of a confirmed taker of morphine. The patient during eleven years had used the drug, and his regular dosage was from 30 to 60 grains a day. The immediate urgency for treatment was an acute maniacal attack. The morphine was withdrawn and $\frac{1}{100}$ grain doses of hyoscine hydrobromate administered every hour. After twenty-five days the patient made a complete recovery, and has remained free from the use of the drug for eleven months.—*Medical News*, 1902, vol. lxxxi. p. 1013.

OBSTETRICS.

UNDER THE CHARGE OF

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Hydatid Mole.—In the *Journal of Obstetrics of the British Empire*, November, 1902, HART contributes an interesting paper upon this subject. He considers, first, the structure of the early normal villus, and draws attention to the relative position of Langhan's layer and of the syncytium, and also Nitabuch's fibrin layer. He believes that both the layers covering the villus are fœtal and ectodermic in origin. He calls attention to the fact that the syncytium and Langhan's layer have no coagulating action on the blood. He believes that normally the early villus has this double epithelial covering, Langhan's layer, and syncytium. These can absorb decidual tissue by penetration, and can pass into bloodvessels without coagulating the blood. Normally their progress is limited by the fibrin layer known as Nitabuch's fibrin layer. The epithelial mantle and connective tissue core, which approximates Wharton's jelly in structure, differentiate in the normal placenta, the syncytium thinning and Langhan's layer flattening, while the connective tissue becomes more fibrous. He estimates that hydatid mole is rare and that in microscopic structure the most notable condition found is the change in the epithelial covering.

The clinical features of hydatid mole consist in the watery or blood-tinged discharge, the enlarged uterus with discharge of vesicles, and the uterine tumor unfixed. Hydatid mole is rarely found in the tube or in the paravaginal tissue.

Hart estimates that in about one-half of recorded cases of syncytioma malignum hydatid mole has preceded the malignant growth. He does not believe that in ordinary cases microscopic examination of a given specimen can determine whether a mole will be followed by deciduoma malignum or not. He is, however, in favor of curetting patients who have had hydatid mole and in whom the uterus remains enlarged, and of carefully examining the scrapings. Should suspicious tissue be found, it will be safer to remove the uterus.

The Fœtal and Maternal Blood Serum.—HALBAN and LANDSTEINER have made a series of experiments upon the serum of maternal and fœtal blood in the Anatomical Institute at Vienna. Their conclusions are as follows: There is a marked difference in the reaction of maternal and fœtal blood in several respects. The serum of the mother's blood requires a larger number of corpuscles to undergo solution than does that of the fœtus. The serum of the mother's blood agglutinates blood corpuscles much more

actively than does that of the fœtus. It has also a stronger action against bacteria and against the process of fermentation. It is also more potent as an antitoxin, and is a more potent agent as an immunizing serum. The active principles of blood serum seem to be present in the blood of the fœtus, but not to be well developed nor to be active. The deficient development of blood serum in the newborn explains the susceptibility of infants to infection. It would be of interest and practical importance to ascertain at what period of extra-uterine life infantile serum becomes active, and how such a result could be brought about.

Intraperitoneal Hemorrhage and Ectopic Gestation.—In the *Journal of Obstetrics of the British Empire*, November, 1902, CULLINGWORTH publishes his lecture upon this subject. The purpose of his lecture is to call attention to the essential points of diagnosis in these cases.

He first describes the symptoms in a case of intraperitoneal hemorrhage following the rupture of an ectopic gestation. He considers the following diagnostic points in these cases as of especial value:

1. The fact that at the moment of attack the patient was in her usual health. This renders it improbable that the hemorrhage was the result of previous chronic disease.
2. Gradually increasing pallor of the patient and the gradually rising pulse rate without rise of temperature.
3. The extreme tenderness of the abdomen.
4. Evidence of derangement of menstruation. For such a condition he believes immediate operation imperative.

In considering pelvic hematocele he believes the majority of cases due to ruptured ectopic gestation. Irregular hemorrhages and pain are almost equally constant symptoms. The appearances of decidua in the vaginal discharges may escape observation. Faintness, nausea and vomiting, rise of temperature, and retention of urine are less constant symptoms of secondary importance. As regards the physical signs of hematocele, an irregular, tender, fixed swelling behind the uterus, pushing that organ forward and to one side, is the condition usually present. The tumor bulges into the rectum and extends laterally into one or other of the pelvic fossæ. When much blood is effused the swelling may reach upward into the abdomen, often higher than the fundus uteri, and sometimes nearly to the umbilicus. At first the outline of the swelling is difficult to make out, owing to the general abdominal distention, the rigidity of the muscles, and great tenderness. In a few days these conditions are altered and the parts are more relaxed. The uterus is usually a little enlarged, displaced forward, and adherent posteriorly. Irregular hardness is felt in the tumor, caused by the adherent pelvic viscera. At times Douglas' cul-de-sac is empty, and the swelling is entirely at the sides.

Pelvic hematocele must be distinguished from retroversion of the gravid uterus, ordinary abortion, inflammation of the uterine appendages, with or without a new growth, or an unsuspected ovarian cyst, with sudden twisting of the pedicle. It may be differentiated from a retroverted uterus by the consistence and by the rhythmic contractions of the pregnant uterus. It is evident that an effort to replace a hematocele under the supposition that

it is a retroverted pregnant uterus may result in its rupture and in fresh and extensive hemorrhage.

In distinguishing pelvic hematocele from ordinary abortion there is with ordinary abortion very free hemorrhage and the passage of clots, while with ectopic gestation and hematocele there is seldom much bleeding, and clots are not discharged.

All physicians of wide experience have met cases in which it was absolutely impossible to clearly distinguish between ruptured ectopic gestation and hematocele or inflammatory disease of the uterine appendages. Fortunately a condition sufficiently severe to justify abdominal section in either case should be dealt with by section, and so there can be no reasonable doubt regarding the best course of treatment.

These remarks apply to torsion of the pedicle in ovarian cyst which had not been diagnosed. In any obscure condition in which the symptoms indicate a grave lesion, abdominal section is safer than continued uncertainty, with possibly concealed hemorrhage.

In discussing how it is that the ectopic ovum causes hemorrhage, Cullingworth calls attention to our modern knowledge regarding the embedding of the ovum, which explains the tendency to perforation of the tube and to a continuation of the hemorrhage unless the tube be removed.

GYNECOLOGY.

UNDER THE CHARGE OF

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ASSISTED BY

WILLIAM E. STUDDIFORD, M.D.

Surgical Treatment of Parametric Cicatrices.—Ott (*Journ. akusch. i shensk. Colesnej.; Centralblatt fur Gynäkologie*, 1902, No. 32) while believing that pelvic massage is the best treatment for old indurations in the broad ligaments, has found that some cases are only relieved by operation. The object aimed at should be the complete division of all cicatricial bands, with suture of the wound in the direction opposite to its long axis, in order to prevent subsequent contraction. The greatest care is necessary while working in the broad ligaments in order to avoid injury to the vessels and ureters. It may be necessary to catheterize the latter as a preliminary step.

The writer has usually obtained union by first intention, but when the wounds heal by granulation, as shown by the persistence of the cicatricial bands, early massage is indicated.

Results of Myomectomy and Castration.—Sauer in his inaugural dissertation (*Centralblatt fur Gynäkologie*, 1902, No. 34) analyzes 104 cases, including 62 abdominal sections, 21 vaginal hysterectomies, and 21 castrations

for fibroids. Supravaginal amputation was performed in all but one of the laparotomies. All the cases of myomectomy and hysteromyomectomy were followed by satisfactory results. As a rule, the tumor diminished in size after removal of the ovaries. Climacteric disturbances were rare after total extirpation of the uterus, whether the adnexæ were left or not. They were common after castration and supravaginal amputation. No psychical disturbances were noted.

The Relation of Dyspepsia to Pelvic Disease.—Sommer (*Centralblatt für Innere Medicin*, 1902, No. 2) made a careful study of twenty-three cases of functional stomach trouble, with a view to deciding the question of their reflex origin. General relaxation of the abdominal viscera and uterine displacements were commonly present. Hyperchlorhydria was most frequently noted. In only two cases was improvement in the pelvic condition followed by relief of the gastric symptoms. In one instance, on the contrary, replacement of a retroverted uterus increased the dyspepsia. In conclusion, the writer states that no connection could be traced between the pelvic trouble and the secretory disturbances.

Sounding of the Tubes.—Ahlfeld (*Centralblatt für Gynäkologie*, 1902, No. 41) reaffirms his opinion that in certain cases in which the sound appears to have perforated the uterine wall it is really introduced into a Fallopian tube. He adds the following case to five others previously reported: A nullipara, aged twenty years, had a movable retroflexion. A sound was introduced, two and four-fifth inches, until it touched the fundus uteri. On turning the point toward the left corner it slipped in one and one-fifth inches farther without meeting any resistance. The same phenomenon was carefully noted later with the patient under anæsthesia. Three weeks after ventrofixation was performed, when the tube was found to be of normal calibre and no evidence of any old or recent lesion of the uterus could be found, hence there could have been no perforation.

Lymphosarcoma of the Uterus.—Wagner (*Centralblatt für Gynäkologie*, 1903, No. 43) reports a case of this rare uterine neoplasm removed by autopsy from a woman, aged sixty-two years. The entire uterus, tubes, parametria, and pelvic and inguinal glands were involved. According to Kundrat, who examined the specimen, the disease must have begun in the lymphoid tissue of the endometrium and extended to the muscular layers. The fact that only three cases of lymphosarcoma of the uterus have been described, is explained by the fact that pre-existing lymphoid tissue is rarely developed in this organ.

This form of neoplasm does not show the same tendency to retrograde metamorphosis and suppuration as cancer. It is beyond the reach of surgery.

Profuse Hemorrhage from a Ruptured Ovisac.—Gottschalk (*Centralblatt für Gynäkologie*, 1903, No. 49) reports a case of intraperitoneal hemorrhage in which he removed from the abdominal cavity a clot, in the centre of which was an ovum the size of a pea, with typical chorionic villi and two

normal fimbriæ. A ruptured Graffian follicle was found surrounded by enormously dilated bloodvessels, the same as those at a placental site. No villi were found in the follicle. It was evident that there was an active hyperæmia and vascular dilatation in the neighborhood of the ruptured follicle. The corresponding Fallopian tube was normal, except that the two fimbriæ found in the clot were missing. According to the writer, as well as in the opinion of his colleagues, the case was one of true ovarian pregnancy.

Extirpation of the Uterus and Vagina for Procidentia.—Miranda (*Arch. di Ost. e Gin.; Centralblatt für Gynäkologie*, 1903, No. 49) adds the following case to twelve already reported by different operators: The patient, aged sixty-three years, had had complete procidentia for twenty years. A circular incision was carried around the vulva and two vaginal flaps were formed by making vertical incisions anteriorly and posteriorly. The cul-de-sac of Douglas was opened and the peritoneum was sutured to the edge of the skin. The bladder was then separated, the uterus removed, and the peritoneal opening was closed. The patient made a good recovery.

Pruritus Vulvæ.—Seeligmann (*Deutsche med. Wochenschrift*, 1902, No. 9) believes that he has found the cause of this affection (excluding cases due to acid secretions, diabetes, masturbation, etc.) in the shape of a diplococcus resembling the gonococcus in shape and appearance. His treatment consists in applications of guaiacol vasogen in 10 per cent. solution, which may be increased to 15 or 20 per cent. It is applied in compresses at bedtime for several nights, and seldom fails to give relief. If there is a return of the itching one or two applications seldom fail to effect a cure.

Urethral Caruncles.—Lange (*Zeitschrift für Geb. u. Gyn.*, Band xlviii., Heft 1) examined 1000 patients with especial reference to the presence of so-called urethral caruncle, and found only 58 undoubted cases, in all of which the growth was excised and examined microscopically. In 20 cases the tumor was a telangiectatic mucous polypus, in 19 granuloma, and in 19 papillary polypus. The term angioma is incorrect as applied to caruncle. The etiology is obscure, though gonorrhœa is undoubtedly a cause of granuloma, and gaping of the meatus in old women may sometimes account for the development of papillary mucous polypi.

These caruncles contain numerous glands, and are distinguished microscopically from prolapse of the urethra by the absence of columnar and transitional epithelium on their surface. By themselves caruncles are painless, the pain accompanying them being due to chronic urethritis, prolapse, or insertion of the pedicle high up in the urethra.

Atrophy of the Uterine Mucosa.—Volk (*Centralblatt für Gynäkologie*, 1902, No. 51) reports the case of a young married woman whose menstruation began at seventeen and continued to be scanty and irregular, but painless, until her marriage, at twenty-two. She was first examined in September, her last period being in February, when she was told that she was four months pregnant, and the diagnosis of pregnancy was confirmed by another physician two months later, though fœtal movements and heart

sounds were absent. Later the diagnosis of uterine fibroid was made, and the tumor (an interstitial growth) was removed, and an examination of the enlarged uterine cavity showed that it was entirely devoid of mucous membrane. Under the microscope the mucosa appeared to have been replaced by loose connective tissue infiltrated with round cells. Near the surface of this cell were isolated cells of an epithelioid type, with indistinct outlines and protoplasm, which took a faint stain with eosin. There was no trace of true epithelium or glands. The muscular layers were unchanged. The ovaries contained numerous dilated lymph spaces lined with endothelium, a few follicles, and numerous corpora fibrosa.

The condition of the mucosa accounted, in the writer's opinion, for the absence of bleeding. The atrophy might be explained by the stretching of the endometrium due to rapid growth of the tumor, as there was no evidence of any inflammatory process. The persistence of ovulation without accompanying menstruation or menstrual molimena was interesting. The fact that the patient had scarlet fever in childhood may account for the beginning of the atrophic process.

Primary Cancer of the Fallopian Tube.—Graefe (*Centralblatt für Gynäkologie*, 1902, No. 51) adds the following case to the fifty-two collected by Zangemeister: A nullipara, aged fifty-one years, came to the clinic with a metrorrhagia of six weeks' standing. She complained only of gradual loss of health and vesical tenesmus. The uterus was retroflexed, and a mass, the size of the fist, was felt behind it. She refused operation, and improved under palliative treatment continued for four months. She was then lost sight of from May, 1900, until February, 1902, during which time she was in good health, when she had an attack of abdominal pain with intestinal obstruction. On examination, the tumor previously felt (originally diagnosed as an enlarged tube, possibly malignant) was unchanged, but at the right horn of the uterus was discovered a tumor larger than a child's head. On opening the abdomen an intraligamentary ovarian cystoma was found on the right side, while on the left was a tube the size of the fist, which closely resembled a hydrosalpinx. On section the sac was filled with papillary growths rich in bloodvessels, which were shown microscopically to be malignant. The muscular wall of the tube was invaded, but not perforated at any point.

The writer believes that the papillary carcinoma was undoubtedly present two years and a half before, when he first examined the patient, as shown by the presence of the sanguineous discharge which had then awakened his suspicions, the stoppage of the flow being due to closure of the uterine ostium. The patient was in good health eight months after operation, so that it was fair to infer that no metastases had taken place.

The writer thinks that although, as in the case reported, papillary cancer of the tubes is sometimes relatively benign in character, it is not safe to delay operation on account of the absence of symptoms. Every enlarged tube, not of probably gonorrhœal or infectious origin, which does not diminish considerably in size under palliative treatment, should be removed. The reason why recurrence has been so common after the extirpation of cancerous tubes is doubtless due to delayed operation.

DISEASES OF THE LARYNX AND CONTIGUOUS STRUCTURES.

UNDER THE CHARGE OF

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Saddle-back Nose.—Dr. Joseph A. M. Smurl, of Philadelphia, reports (*American Medicine*, January 31, 1903) and illustrates a case of success in subcutaneous injections of solidifying oils to correct a saddle-back nose. He explains his method in detail as the result of more than four years' experimentation with injections of paraffin.

Primary Nasal Diphtheria.—Dr. Helot, of Rouen, reports (*Annales des Maladies de l'Oreille, du Larynx, du Nez et du Pharynx*, January, 1903) two out of a number of cases of observations of primary nasal diphtheria. He states that the infrequency of this malady is only apparent among cases passing unrecognized in the absence of constitutional symptoms.

Dr. Helot has observed several cases of primary nasal diphtheria without propagation to either larynx or pharynx, the affection in some instances remaining localized in a single nasal passage. Of the two cases reported, one was an example of toxic diphtheritic fibrinous rhinitis, and the other of diphtheritic fibrinous rhinitis without general symptoms. The exact clinical diagnosis, it is stated, cannot be made without bacteriological culture.

Parotiditis.—Dr. Douglas Symmers, of Philadelphia, contributes an illustrated paper (*American Medicine*, January 31, 1903) on the "Chronic Bilateral Parotiditis among the Insane, with a Detailed Account of Five Cases." Each of these cases, it is shown, has several points in common with the others. All were above thirty years of age, and exhibited more or less stigmata of degeneration. Three were almost unquestionably syphilitic, and, with the exception of one case, nephritis had been proved to exist or was strongly suspected. Dr. Symmers refers to Dr. Kyle's opinion that substances in the saliva may be causative of certain enlargements of the thyroid glands, and deems it quite probable that certain cases of syphilis, nephritis, and other morbid conditions are attended by the elaboration of irritant substances in the saliva which bear the selective affinity for the structures of the parotid glands.

Removal of an Accessory Thyroid Tumor at the Base of the Tongue.—Dr. Randolph Winslow, Professor of Surgery in the University of Maryland (*American Medicine*, December 13, 1902), removed a thyroid tumor from the base of the tongue of a girl, aged seventeen years, through an external incision made in the median line from the chin to the hyoid bone, cutting through the mylohyoid muscle and separating the geniohyoid and geniohyoglossi muscles until the base of the tumor was reached, whence it

was enucleated with the aid of an assistant's fingers in the mouth, pressing the tumor down. The covering mucous membrane was removed through the wound with scissors, leaving a large opening communicating with the mouth. This was closed with catgut, as were the separated muscles, and the skin incision was sutured with a subcutaneous silkworm-gut strand. Healing took place by first intention. The growth was about one-half the size of a hen's egg, and its thyroid character was demonstrated by microscopic inspection. Some general remarks and a bibliography conclude the article.

Primary Tuberculosis of the Tongue.—In an illustrated paper on "The Early Appearances, Diagnosis, and Treatment of Tuberculosis of the Upper Air Tract" (*Journal of the American Medical Association*, February 21, 1903), DR. WALTER F. CHAPPELL, of New York, reports a case of presumptive primary tuberculosis of the tongue which preceded by two years any discoverable evidence of pulmonary tuberculosis.

Foreign Bodies (Coins) in the Œsophagus of Infants.—PROF. PIERRE SEBILEAU, of the Hospital Larboisière, contributes (*Annales des Maladies de l'Oreille, du Larynx, du Nez et du Pharynx*, January, 1903) an article on external œsophagotomy in the infant for the extraction of coins in which he emphasizes several points to which we desire to call attention. In most of these cases radiography revealed the positions of the coins transversely impacted at the upper constriction of the œsophagus. In one case out of the five reported, and in which the œsophagus was larger, the coin had passed the first constriction and had become engaged in the thorax in the second constriction, about the level of the bronchial root of the lung. Four of these cases were successfully operated upon. In all of them it was found that the lesions in the œsophagus were confined to the lateral walls which had been subjected to pressure.

In a child, aged three years, in whom a sou-piece had remained for twenty-five days, solid adhesions had become established between the œsophagus and the walls of the primitive carotid artery. These adhesions had occupied the extent of a centimetre, and were a little above the foreign body, which had probably been forced down some two centimetres by contractions of the canal and the force of the alimentary bolus upon the thinned walls at point of impact. The walls of the adhesions were very thin, reduced to a single mucous covering, and confounded with the peri-œsophageal conjunctive tissue.

In a child, aged three years, who had swallowed a five-centime-piece five weeks before the operation, the lesions were identical, but a little less advanced. In a child, aged two years, in whom a five-centime-piece had been in position but ten days, the lateral peri-œsophagitis was still less advanced, but of the same nature. The œsophageal wall was unrecognizable, extraordinarily friable, and enclosed in a sort of reddish, inflammatory mass which extended from the median line to the vessels. Another point made is that skiagraphy should supersede the exploratory procedures with œsophageal probes and extractors. When the operation is not performed immediately after the location of the foreign body a final skiagraphy should be made immediately before the operation. In one instance in which radiog-

raphy revealed the coin in the thorax and in front of the third and fourth dorsal vertebræ, the œsophagotomy was practised the following morning, but it was impossible to find the foreign body, and the wound had to be closed. The child was immediately re-radiographed, and the coin was discovered to have descended into the abdomen.

There are a number of other interesting points in this paper, chiefly of surgical interest.

Falsetto Voice.—A paper on "The Falsetto Voice; Origin and Respiratory Treatment; Dental Irregularities," is contributed by Dr. Marcel Natier, of Paris, to the February number of *The Laryngoscope*. This has reference to the falsetto or sometimes called eunuchoid voice of male adolescents and adults. Dr. Natier recognizes that the condition is referable to a profound disturbance of the respiratory function, and illustrates his contention by a series of tracings of the respiration during those ordinary phases and during the emission of vocal sounds. He agrees with the majority of observers that respiratory gymnastics constitute the most efficacious and most rapid plan of treatment.

[The collator has for many years found that the habit of speaking in this peculiar voice can be broken by teaching the individual to speak with distended abdomen. This distention of the abdomen forces the diaphragm downward, lengthens the column of air in the trachea and larynx, and thus lowers the pitch of the voice. It is difficult to speak in a falsetto voice when the abdomen is thus distended.]

Sarcoma of the Maxillary Sinus.—Prof. Joseph S. Gibb, of Philadelphia, reports (*Journal of the American Medical Association*, February 21, 1903) a case of sarcoma of the maxillary sinus in which excision of the jaw was practised and on which he takes occasion to make a few general remarks. In this instance the rapidity of the growth was unusual. In six weeks from the time of the first manifestation of the disease the entire antrum, with a large portion of the left nasal chamber, was filled with the new-growth. Degeneration and liquefaction of the growth had taken place, and the osseous tissues were involved from pressure and absorption. After a first operation, which was the incomplete excision of the upper jaw, recurrence was noticed in seventeen days, and in four weeks' time the entire cavity became filled and the growth projected into the mouth. In a second operation the external carotid artery was then ligated and the upper jaw completely excised. The patient reacted well, and had shown no evidence of recurrence at the time of the report.

Lupus of the Epiglottis.—Dr. Talbot R. Chambers, of Jersey City, N. J., reports (*The Laryngoscope*, February, 1903) a case of excision of the epiglottis for lupus in a Swedish girl, aged twenty-one years. Under chloroform vaporized by oxygen gas the excision was performed with a so-called Brandigee adenoid forceps, and adrenalin was swabbed in the wound to control the bleeding. Under the free applications of cocaine and adrenalin twelve days later a small lump of tumor was excised with the same forceps from the right epiglotto-tonsillar membrane.

A résumé of a few recorded cases in the literature accompanies the report.

OTOLOGY.

UNDER THE CHARGE OF

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Contribution to the Bacteriology of Otitis of Measles.—ALBESHEIM, of Berlin. Scheibe, through experiments by cultures and inoculations, always found pyogenic organisms in the secretions after paracentesis. Most frequent in pure cultures were streptococci, half as frequent were staphylococci albi, and somewhat rarer staphylococcus aureus. Sweigerhofer found in two cases streptococci pyogenes and staphylococcus aureus by culture and inoculation, besides, microscopically, streptococci six times, once together with staphylococci; likewise microscopically Moos got streptococci. Netter found the same; likewise in a lethal pyæmic case staphylococcus aureus and two kinds of bacilli. Zaufal cultivated—whether in pure cultures is not stated—staphylococcus aureus once. Wolff found the pneumococcus pure once, twice staphylococcus and streptococcus. Williams and Councilman obtained diphtheria bacilli in two cases of rubeola in which the throat was free.

To these cases Albesheim adds five cases. Paracentesis was done by a needle sterilized in the flame or with the galvanocautery point. Cultures were made in gelatin and agar-agar tubes. Then the contents of these tubes were poured into Petri dishes. In one case he used the water of condensation method. The gelatin plates were kept at room temperature; the agar-agar plates in the thermostat, 37° C. From the dishes existing colonies were carried over to agar-slants, and from these to another dish to get pure cultures. The biological characteristics were studied by observations on different medias and animal inoculations were made. Two smear preparations were made in each case; one stained by methylene-blue or fuchsin, the other by Gram's method.

To sum up: He found streptococcus once in pure culture; once the staphylococcus albus. Once the streptococcus was associated microscopically with a bacillus which could not be demonstrated through culture experiments. Once staphylococcus albus, together with a bacillus, were seen on a smear, but the bacteria could not be cultivated. The same picture occurred again with staphylococcus albus. The bacilli of this last case of mixed injection could be cultivated. The bacilli were small, with rounded ends, motile, and generally took the basic aniline colors well, and were intensely colored by Gram's. Flagella could not be demonstrated. The bacilli grew at room temperature and in the thermostat 37° C.; in the latter faster. On gelatin

plates it formed small white round colonies after three to twenty-four hours, causing shell-shaped liquefaction. Microscopically the superficial as well as the deep colonies appear rounded or whetstone like, have a thin border, and are finely granular. In the gelatin stab they form a thick white thread; on the surface a lardaceous, whitish coating. Here also liquefaction begins in from three to twenty-four hours. After some days the whole tube became filled with a cloudy liquid, at the bottom of which lay a compact white mass and a thin skin floating on the surface. On agar the growth is similar to that on gelatin. In grape-sugar agar gas formation failed. Bouillon was clouded in twenty-four hours, forming a cloudy sediment; after four days a delicate membrane was seen on the surface. Milk was not coagulated. The bacillus is not pathogenic for mice. Albesheim could not identify these bacteria, but they can be classified in the group of Migula.—*Archiv f. Ohrenheilkunde*, 1901, Bd. liii., S. 87–99.

Neuroses and Mastoid Operations.—Muller (*Arch. f. Ohrenheilkunde*, Bd. liv., Heft 3 and 4) reports ten cases of chronic purulent middle-ear inflammation in which the radical operation was performed. In all of the cases a complicating neurosis was present. Two cases were complicated with epilepsy, one with chorea, one with hystero-epilepsy, four with hysteria, one with menstrual dementia, and one with multiple sclerosis. (The last case the author admits is not a neurosis.)

In one case, that complicated with chorea, apparently a permanent cure of the complication followed the operation immediately. In the other cases an improvement in the symptoms of the complicating disease took place. The improvement, however, was only temporary in a large proportion. Muller does not believe that the various neuroses were causally connected with the ear trouble, for in all of the cases the ear trouble antedated by years the nervous disease; moreover, the improvement followed immediately upon the operation when the ear trouble was far from healed. The improvement should, according to Muller, be ascribed to the mastoid operation itself, and he proposes as causal factors:

1. The narcosis and shock of the operation.
2. The loss of blood during the operation.
3. The influence of the after-treatment.

By the narcosis and shock of the operation Muller conceives that the general organism and psychical nature are upset to an extent sufficient to throw the neurosis temporarily in the background. More importance is attached to the last two factors—namely, the loss of blood and the after-treatment. Since in all the operations the dura was exposed over a greater or less extent, the effect of both the loss of blood and of the after-treatment is to alter the blood supply to the brain substance. Together with the change in the blood supply goes a change in the nourishment, and therefore function of the nervous elements.

DERMATOLOGY

UNDER THE CHARGE OF

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A Case of Favus of the Scrotum Co-existing with Ringworm of the Thigh, Giving Identical Trichophyton-like Cultures.—MEWBORN (*Journal of Cutaneous Diseases*, January, 1903) reports the case of a mulatto, aged twenty-two years, who had a palm-sized, red, scaly, sharply-defined patch with a papulo-vesicular border in the genito crural region, and several smaller scaly patches in the right inguinal region on the abdomen, the buttocks, and in both axillæ. At the same time, on the anterior surface of the scrotum there was a chain of typical favus cups presenting the usual features. Microscopic examination of the scrapings from the scaly patches showed a fungus presenting the features of the trichophyton, while the favus cups presented an entirely different picture, corresponding to the types of fungus found in favus of the scalp. Cultures were made from the patches and from the favus cups on glucose agar, and kept at the ordinary room temperature. At the end of a week the growth obtained from the cups was indistinguishable from that made from the ringworm patch. Attempts to inoculate the favus cultures on the author's arm and on mice were unsuccessful, but inoculations with the trichophyton cultures succeeded upon a rabbit, favus cups appearing at the end of a week. The author concludes from this case that the same trichophyton, on the same patient, but in different parts of the body, produced two clinically distinct diseases—favus and ringworm.

Dermatitis Coccidioides.—MONTGOMERY, RYFKOGEL, and MORROW (*Journal of Cutaneous Diseases*, January, 1903) add a new case of this rare and extremely interesting affection to the small number previously reported. The patient, a man, aged fifty-four years, a native of Switzerland, first came under Dr. Montgomery's observation in January, 1901. He was neither tuberculous nor syphilitic. The trouble for which he sought advice had begun seven years before as an enlargement of the left hand and forearm. These continued to enlarge, and a year later the left leg and ankle began to enlarge. Four years later an eruption appeared upon the chest, remains of which were still present, and in 1900 an eruption had appeared upon the left forearm and hand. There was hypertrophy of the skin and subcutaneous tissue of the left forearm, hand, both legs, and left foot. There was no apparent enlargement of the bones. Over the chest and abdomen there was pigmentation occurring as brown, pea-sized spots, the remains of a previous

papular eruption. On the left forearm and back of the left hand there was an eruption of discrete papules, pustules, and nodules, many of the pustules being covered with crusts. Upon the neck there was a pustular folliculitis forming a boggy mass, and the right ear presented a condition resembling an acute eczema. Upon the left leg there was a superficial elephantiasis with papillary overgrowth.

The patient had been treated for syphilis at various times without benefit, and had taken iodide of potassium in increasing doses without producing any change in the disease. For two months he was treated with the X-rays with decided benefit, the pustules drying up and the nodules becoming flatter; but this treatment had to be interrupted because of the progress of the internal infection. Death occurred one year after the correct diagnosis had been made.

At the autopsy the suprarenal capsules were found to be much enlarged, the normal tissue being replaced by a friable, fairly dense, yellowish-white tissue. The left lung throughout its entire extent and the upper lobe of the right lung contained numerous bodies resembling miliary tubercles. Microscopically the tubercle-like bodies and the suprarenal capsules were found to consist of granulomatous tissue containing numerous giant cells and capsulated bodies, many of the latter being included in the giant-cells. The organism found in the disease presented a double cycle of growth, one in the tissues, the other on culture media, the two cycles having no features in common. In the tissues it occurred as a sphere 3.5 to 5 microns in diameter, surrounded by a clear capsule, the outer wall covered with spines which could only be seen in the fresh specimen. The smaller capsules had clear or granular contents, the larger ones were filled with endogenous spores. Outside of the body the growth was that of a mould fungus. When a sufficient quantity of the culture was employed intraperitoneal inoculations in the guinea-pig were invariably fatal.

The Treatment of Lupus Erythematosus.—Hollander (*Berliner klinische Wochenschrift*, 1902, No. 30) has employed the following method of treatment with very satisfactory results in the severest and most unfavorable cases of erythematous lupus: Large doses of quinine are administered internally, and at the same time the diseased areas are treated locally by applications of tincture of iodine. After having ascertained that the patient has no idiosyncrasy in regard to this drug, a half-gramme of the sulphate or hydrochlorate of quinine is given three times a day, and five to ten minutes after each dose the affected parts are thoroughly painted with iodine. This is continued for five or six days; then the treatment is suspended for an equal period of time, until the crust produced by the iodine has fallen off. If the reaction is slight the dose of the quinine is increased. The result of this treatment is either a scar-like atrophy or a complete return of the skin to the normal, the latter occurring in the recent cases. In the majority of cases about 60 grammes of quinine are necessary to complete the cure.

Alopecia Areata of the Moustache of Dental Origin.—Milian (*Annales de Dermatologie et de Syphiligraphie*, 1902, No. 11), at a séance of the Société Francaise de Dermatologie et de Syphiligraphie, reported the following

interesting case of alopecia areata: A man, aged thirty-five years, who had suffered much from carious teeth, of which he had a great number, presented a patch of alopecia areata in the mustache over the right lateral superior incisor. This tooth, after a severe neuralgia of both jaws, had remained very sensitive, and the patch of alopecia had developed over it at the same time that vesicles, identical in appearance with those of herpes, had appeared on the corresponding part of the gum. The hairs about the borders of the patch were easily extracted, and presented the usual appearances observed in this disease. The skin was thinned and presented a marked anæsthesia. There were no other patches of alopecia. The patient was directed to have the mouth cleansed and the teeth looked after by a dentist, and was given quinine internally in moderate doses. Shortly after the jaws had been put in good condition, the sensitive incisor having been extracted, the patch of alopecia ceased to extend. Later, the neuralgia ceased, the sensibility of the skin returned, and, at the end of about four months, the plaque was completely covered with hair.

Mycosis Fungoides and Its Treatment by the X-rays.—Jamieson (*British Journal of Dermatology*, January, 1903) reports two new cases of this comparatively infrequent affection, in one of which quite remarkable results followed the prolonged use of the X-rays. This case began with the usual eczema-like patches, which were followed in time by tumors which ulcerated. Soon after coming under the author's care treatment with the X-rays was begun, the exposures lasting from three to five minutes, with a soft tube at a distance of four inches. This treatment resulted in a steady and continuous shrinkage of the tumors, although new lesions appeared in the parts not exposed to the rays. After sixty exposures, on as many different days, all the tumors had disappeared. Reaction sufficiently marked to require suspension of the treatment was at no time manifest. Not only did the tumors disappear, but the thickened patches were also removed, and with them the itching.

Acute Symmetrical Erythematous Keratodermia Caused by the Administration of Arsenic.—White (*British Journal of Dermatology*, January, 1903) reports the following case: A boy, aged thirteen years, suffering from a severe chorea, was given 4 minims of liquor arsenicalis every four hours, and later the dose was increased until he was taking 10 minims every four hours. At the end of ten days the physiological effects of the drug, such as conjunctivitis, coryza, white-coated tongue, became manifest. The drug was now stopped. Erythematous symmetrical patches then appeared over all the metacarpophalangeal and phalangeal joints, and the thenar and hypothenar eminences appeared as lemon-colored islands surrounded by erythematous rings. Erythematous zones appeared upon the flexor aspects of the wrists, upon the extensor surfaces of the elbows, and upon all points subjected to pressure, as the spines of the scapulæ, the buttocks, and the great trochanters. The bony prominences of the legs and feet were similarly affected, and the soles presented appearances similar to those of the hands. All these zones were symmetrically circular, rose-pink in color, fading away toward the margins, which were well-defined; they were tender to the touch,

and the skin was considerably thickened. Over the entire body was a scarlet rash resembling that of mild scarlatina. Two days later tenderness had disappeared, the affected zones became darker and began to desquamate. The mucous membrane of the lips also began to desquamate, and the alæ nasi were thickened and irritable. Two or three weeks later the patient was discharged, cured of his chorea, and without any trace of arsenical pigmentation. Altogether the patient had taken 3.5 grains of arsenious anhydride. As the author has seen a number of similar cases in children taking large doses of arsenic, he is of the opinion that they are commoner than is generally supposed.

Erythema Scarlatiniforme Desquamativum Recidivans.—KRAMSZTYK (*Dermatologische Zeitschrift*, Band ix., Heft 3) reports three cases of this interesting affection, in the first two of which nine attacks occurred, and in the other two, two and three attacks respectively. In first attacks the diagnosis between this disease and scarlatina may be difficult. The absence of the pharyngeal redness and the strawberry tongue characteristic of the latter are of great value in the differential diagnosis, although these are occasionally seen in the former affection. Even such complications as inflammation of the ears and nephritis may occur, so that the only certain diagnostic feature is the recurrence of the eruption. The author believes that the disease is not a local affection of the skin, but a general infection to be classed with the other infectious exanthemata; it is not an erythema scarlatiniforme, but a "pseudoscarlatina recurrens."

Syphilitic Erythema Nodosum.—MARCUSE (*Archiv für Dermatologie und Syphilis*, Band lxiii., Heft 1) reports three cases presenting an eruption resembling, more or less closely, ordinary erythema nodosum, in which symptoms of secondary syphilis were also present. In all three cases, besides many lesions which resembled opened furuncles, there were softened nodes like gummata, and solid ones resembling the lesions of erythema nodosum. Histological examination of an excised node revealed a phlebitis undergoing transformation into a granulation tumor presenting the characteristics of a gumma. The author's conclusions, from a study of his own cases and those reported by other observers, are as follows: In rare and relatively severe cases of syphilis an erythema nodosum-like eruption appears in those regions of the body for which erythema nodosum shows a preference, which, as a rule, should be regarded as a specific form of exanthem, and is best designated as a "nodose syphilide," as is done by the French. This nodose syphilide usually appears in the first year after infection and is often associated with other secondary skin manifestations. Its course is varied; in some cases it disappears without leaving any trace; in others softening and ulceration occur. On clinical grounds, as well as from pathologico-anatomical investigation, it is probable that these lesions have their origin in the subcutaneous veins. There are great analogies, clinically as well as anatomically, between this eruption and certain nodose "tuberculides" which have their origin in the veins. Upon clinical grounds it is probable that this form of eruption must sometimes be regarded as belonging to the secondary period, sometimes to the tertiary, and occasionally as intermediate between the two.

PATHOLOGY AND BACTERIOLOGY.

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On Changes in the Bacteriolytic Power of the Blood after Typhoid Vaccination, and On the Protective Value of Antityphoid Vaccination.—WRIGHT (*The Lancet*, September 14, 1901, 715; *Ibid.*, September 6, 1902) shows that injections of an amount of vaccine sufficient to cause a marked reaction are followed by a decreased bacteriolytic power in the patient's blood against the typhoid bacilli, as can be shown *in vitro*, and as unfortunately has been shown practically by the greater susceptibility of such recently vaccinated patients to typhoid infection. This period of diminished resistance is followed by a marked increase of bacteriolytic power over the normal. To obviate such difficulties the author advises smaller doses at first, which are found to increase at once the patient's bacteriolytic power, and which may then be followed by larger doses. In his second paper Wright discusses the tabulated results of the thousands of soldiers, who, in the past few years, have been vaccinated against typhoid before going to regions of infection. He finds that the mortality and also the liability to infection of vaccinated over unvaccinated men is reduced to from two to twenty-eight fold.—F. P. G.

The Influence of Mode of Introduction on the Preventive and Curative Action of Tetanus Antitoxin.—DESCOSS and BARTHELEMY (*Jour. de Physiologie et Pathologie Générale*, 1902, vol. iv., No. 5), in experimenting on rabbits with a strong tetanus antitoxin, find the preventive dose given twenty-four hours before injection of tetanus toxin is equally efficacious, whether injected intraperitoneally, intracranially, intradurally, subcutaneously, or intravenously. When the antitoxin is given twenty-four hours after the toxins, that is, during the beginning period of contractures, the intraperitoneal injection is worthless, and the intravenous injections are by far the best. In the period of full tetanus, forty-eight hours after the toxins, the subdural method alone will save. The authors suggest from these results the use of the intravenous injections in cases of tetanus treated with antitoxin during the incubation period.—F. P. G.

Preliminary Report of the Appearance in the Philippine Islands of a Disease Clinically Resembling Glanders.—R. P. STRONG (Bureau of Government Laboratories, Manila, 1902) discusses the findings in a malady

affecting horses, and more rarely cattle, in Manila, which was at first taken for farcy, the cutaneous form of glanders. The disease starts as a slight abrasion in the skin and spreads along the lymphatics, forming subsequently abscesses in the glands. It may secondarily reach the nares, but never occurs there primarily. It is not usually fatal. On microscopic examination the etiological factor is found to be a blastomyces, which is grown with difficulty on artificial media and will reproduce the characteristic lesion in monkeys. The causative organism is not to be mistaken for the mould fungus causing "bursattee" in India, but is closely allied in all probability to the "saccharomyces farcinomosus" described by Tokishiga as the cause of lymphangitis in epizootica in Japan. The treatment recommended is the cleansing of the skin with some antiseptic solution and opening of the tumors, followed by curetting and irrigation.—F. P. G.

The Serumtherapy of Typhoid Fever.—CHANTEMESSE (*La Presse Médicale*, 1902, vol. ii., No. 103, p. 1227) presents a carefully tabulated account of the percentage of mortality in cases of typhoid fever in Paris during twenty months, which have received the ordinary medical treatment, including cold baths, in comparison with the cases treated by antityphoid serum and cold baths. In the General Paris Hospital the number of cases under ordinary treatment was 1192 with 286 deaths, that is, a mortality of 19.3 per cent. In the Bastion hospital where the serum treatment was adopted the cases numbered 179, with a mortality of 3.7 per cent. In the Saint Mandier Hospital of 151 cases treated with serum the mortality was under 6 per cent. The disease has been of an unusual virulence during this period. The fatal cases at the Bastion were attributable in most cases to intestinal perforation. Experimental results on guinea-pigs show that the serum has the power of preventing and curing fatal doses of the living typhoid organism or of the typhoid toxines.—F. P. G.

A Study of an Hæmolytic Complement Found in the Serum of the Rabbit.—SWEET (*Univ. of Penna. Med. Bulletin*, December, 1902, vol. xv.), as the result of a most painstaking research, comes to the following conclusion in regard to the complement in rabbit's serum necessary to complete the hæmolysis of bovine erythrocytes which have been sensibilized with artificially produced rabbit's immune body:

1. The complement content of the serum may be increased by the injection of certain chemiotactic substances such as aleuronat and oil of turpentine.

2. The complement is not secreted by leucocytes, but exists in the circulating plasma.

3. It does not occur in the normal aqueous fluid of the anterior chamber of the eye, but is present in the transudate which fills the chamber after the normal aqueous fluid has been withdrawn. This newly-formed fluid contains no leucocytes, and the complement contained in it is due to abnormal pressure osmosis of the ciliary vessels owing to decreased intraocular pressure.

4. An artificially prepared plasma contains complement.

5. The artificially increased natural resistance in the peritoneum of animals caused by previous injections of such fluids as bouillon is probably due to similar changed osmotic conditions which allow the passage of complement from the circulating blood.—F. P. G.

The Relationship Between Human and Bovine Tuberculosis.—J. G. ADAMI (*Manchester Medical Chronicle*, March, 1902) has confessed himself to be of an open mind on many of the points involved in this discussion, which was brought to a height by Koch's rather startling paper before the London Congress of Tuberculosis in 1901; but after a full and judicious review of the work of others, and from his own experience, he ventures pretty definite conclusions on the more important points in question.

Bovine tuberculosis can be and usually is transmitted from cattle to cattle by inhalation or contamination of the various discharges. Human tuberculosis is likewise transmissible to cattle, but is not markedly virulent except as a mixed infection. Certain breeds of swine seem to show more marked susceptibility than others to this form of infection.

Human tuberculosis is usually transmitted from man to man, and the organisms of human tuberculosis vary somewhat culturally and pathogenically from the bovine variety, but not to the point that we should be justified in regarding the two as different species.

Bovine tuberculosis may be transmitted from cattle to man either through wounds or through the alimentary canal by food, the latter form of infection being almost entirely limited to children. Milk infections probably take place only in cases of advanced disease in animals in which large numbers of bacilli are present. Animals showing either physical signs of tuberculosis or reaction to tuberculin should be killed.—F. P. G.

Agglutination in Mixed Infections, and Their Means of Diagnosis.—CASTELLANI (*Zeitschrift für Hygiene*, 1902, Band xl. p. 1) has experimentally shown the coexistence of several specific agglutination properties in the blood of mixed infection, and has indicated a method which may prove of great value in the diagnosis of infections due to more than one microorganism. The work has been done principally on rabbits, and the organisms chiefly used were the B. typhosus, B. coli, and B. pseudodysenteriæ (Kruse). He finds in experimental mixed infections brought about by the inoculaton of subminimal lethal doses of living bouillon cultures that the blood of the animal acquires agglutinative properties for each of the organisms—properties equal in onset, intensity, and duration to such properties as existing in an infection caused by any single organism. When a second infection follows the first after a lapse of time, the agglutinative power for the second organism follows the regular course, and the agglutination for the first organism is in nowise affected. In mixed infections in man the several specific agglutination properties are found to be present. This would readily serve for the diagnosis of mixed infections if it were not for the fact that normal agglutinative properties may exist in the blood for organisms other than that causing the infection. To obviate this the author has devised the following scheme: He finds that when 2 or 3 c.c. of serum of an animal infected with a single organism are placed for twenty-four

hours with a considerable mass of the causative organism, these will settle to the bottom, and the serum—before this treatment highly agglutinative—will lose not only all agglutinative power for the causative organism, but also its natural agglutinative properties for other organisms. With the serum, however, of an animal infected or immunized with two or more organisms (A and B), saturation with A, for example, will remove all the agglutinative properties for A, but in nowise affect those of B.—F. P. G.

Presence of the Bacillus of Eberth in the Blood of Typhoid Fever Patients.—M. Busquet (*La Presse Médicale*, 1902, No. 50, p. 593) records forty-three cases of typhoid fever, in all of which he was able to isolate the typhoid bacillus from the blood during life. In thirty-three examinations the result was positive in the first culture, seven times in the second culture, twice in the third culture, and once the organism was not obtained until the fourth trial. The bacillus was obtained twenty-two times between the fourth and seventh days, sixteen times during the second week, and five times during the third week. It was, moreover, isolated from the blood in eight cases before the Widal reaction was positive. In only twenty-nine of the forty-three cases was the typhoid bacillus found alone, for in the other cases organisms such as the pneumococcus, streptococcus pyogenes, and staphylococcus pyogenes aureus were likewise present. Most of the cases with mixed infections were either clinically atypical or exceedingly severe. The technique was similar to that described by Cole, etc., except that only 1 to 5 c.c. of blood was used, and this amount was distributed among twenty to thirty flasks, containing 250 c.c. of bouillon each.

Busquet draws particular attention to the clinical value of this method of diagnosis in atypical cases of typhoid fevers, and also dwells on its use as a means of early diagnosis. He believes it especially helpful in cases when the Widal reaction is delayed. Such methods are, of course, not available for private practice, but in large, well-equipped hospitals the author thinks their adoption would be of great advantage.—W. T. L.

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AMYOTROPHIC LATERAL SCLEROSIS.

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Writing on amyotrophic lateral sclerosis in The American Journal of the Medical Sciences in June, 1896, I said: "The clinical picture which is called up by this name is a well-defined one, and not subject to remarkable variation. So much cannot be said for the pathological process upon which the disease is dependent, nor for the morbid anatomical conditions found at the termination of the disease." The truth of this statement is substantiated by the case which I herewith record. That it is no uncommon experience for the post-mortem investigation of a case to show that the disease clinically typical is not dependent upon the classical lesion, viz., degeneration of both motor neurons, constituting atrophy and disappearance of the anterior horn cells and degeneration of the pyramidal tracts, is abundantly verified by the reports of cases cited in my first paper.

Amyotrophic lateral sclerosis is a rare disease, among the rarest of all organic nervous diseases. In my clinic the diagnosis has been made only six times in five years, during which period about seven thousand new cases of nervous diseases have come under my observation. In view of the fact that recent investigations have shown that some cases reported clinically as typical examples of this disease have been found to be dependent upon syringomyelia, myelitis, and internal hydrocephalus, it is not unlikely that in some of these cases the diagnosis was erroneous. To show further the rarity of the disease in ten years at the City Hospital, where chronic nervous diseases are very common, I have not seen upward of six or seven cases. The disease has been known to physicians for more than a quarter of a century. Char-

cot and Joffroy first described it in 1869, but general knowledge of the disease dates from Charcot's classical description in 1874. Still very little is known of its natural history, and absolutely nothing of its etiology.

Before entering upon some discussion of the nature of the disease and its occurrence, I present the history of a case with clinical and anatomical details, which throws some light upon one or more of the questions concerning the evolution of this disease which are yet unsettled.

Clinical Summary. Woman, aged thirty-six years. First symptoms, pain in neck and head, weakness of the upper extremities and of the muscles that support the head; atrophy and fibrillary twitchings of the muscles of the shoulder girdle, neck, and hands; profound exaggeration of all the tendon jerks; muscular hypertonia; slight spasticity of the lower extremities, and slight contracture of the arms and hands; Babinski phenomenon; no trophic, sensory, or sphincter disturbances; early and profound bulbar manifestations; duration of the disease about three years.—The patient, a married woman, aged thirty-six years, accustomed to housework, came under my observation June 17, 1897. Her family history was not of interest save that her mother died of tuberculosis. No history of nervous disease could be elicited. She had never borne children; her sterility had been attributed to uterine disorder, for which she had received much treatment, five curettements, and one laparotomy. The major operation was in 1892, and one curettage a year since then. When she came to the clinic in June, 1897, she complained of severe frontal headache and pain in the back of the neck radiating to the top of the head; of a tired feeling of the neck and shoulders; of inability to bend the neck forward when sitting with the head leaning back against a rest, and to lift it from the pillow when lying, without the aid of the hands; of profound "nervousness," especially when excited or annoyed; of tremulousness and weakness of the hands, at times of the entire body, and of weariness. A journey like that to the clinic makes her very tired; light housework fatigues her, shopping makes her nervous, depressed, and prostrated; putting up the hair exhausts her.

She cannot fix the time exactly when these symptoms came on, for she has not been in good health for seven years. She is positive that the nervous symptoms have developed within the past two years. In this time she has lost weight steadily, thirty pounds altogether.

Examination at this time showed well-marked atrophy of the right supraspinatus muscle and slight atrophy of all the muscles of the right shoulder, and of the right hypothenar eminence. All of these muscles are the seat of fibrillary twitchings, and their mechanical irritability is much increased. Their response to electrical currents is very sluggish, especially that of the right supraspinatus. The change is a quantitative one, there being no real reaction of degeneration. Inability to use the right upper extremity is proportionate to the atrophy. It was noted that she carried the head peculiarly: in a fixed position, thrown slightly backward, the chin tilted upward. This, taken in connection with the difficulty she has in raising the head when lying, bespeaks involvement of the trapezii muscles. The grip of the right hand is weaker than the left. Both hands seem to have lost their dexterity. The knee-jerks are lively, the right more than the left, both pathologically increased. There is

distinct ankle clonus on the right side, partial on the left side. The gait is not impaired, and she maintains that aside from weakness she walks as well as usual.

Sensibility unimpaired. The functions of the bowels and bladder are undisturbed. Deep pressure does not cause pain, although the atrophying muscles feel sore. The visual fields are normal, and there is no disorder of the special senses. The patient's voice is high-pitched, not modulated, and articulation is slightly impaired. Her features have a set expression, as if the emotional muscles were on the point of acting. (Fig. 1.)

FIG. 1.



Illustrating the "spastic" condition of the emotional muscles.

In the autumn of the same year, six months after the above history was taken, it was noted that the patient complained of dyspnœa, dysarthria, palpitation, easily induced fatigue, dysmenorrhœa, profound nervousness, lack of will power, mental depression, suicidal impulses, increasing helplessness, and of difficulty in swallowing. If food gets on the back of the tongue it must be dislodged with the finger; if she gets it out into the anterior part of the mouth and then shoots the tongue back quickly the bolus goes down. This is exhausting. The face gets tired on chewing and talking. There is occasional regurgitation through the nose. The atrophy of the right shoulder girdle has increased, and extended so that now all of the muscles, including the trapezii, are involved. (Fig. 2.) The hypothenar eminence and other muscles of the hand are not more conspicuously atrophied than before. Fibrillary twitching of the muscles, not only of the atrophied muscles, but of

others of the upper extremity that look normal, is very distressing. Myotatic irritability of all the muscles is very much increased, the knee-, ankle-, elbow-, and jaw-jerks being abrupt and exaggerated. The Babinski reflex is present. The gait is spastic, the stride slight, the strength feeble. The trunk is held rigid, the head fixed and tilted backward. The tongue is the seat of fibrillary tremor, and has the characteristic "bunched" appearance of atrophy. It can be protruded

FIG. 2.



Showing extreme atrophy of shoulders.

just beyond the lips. Intrabuccal motility is now much impaired. The lips have lost their alertness and can no longer be puckered. There is drooling at night. Vocalization and articulation are typical of bulbar paralysis. Attacks of dyspnœa, which are not infrequent, are most distressing to the bystander and agonizing to the patient.

The atrophy which the patient presented at this time is well shown by the accompanying photographs.

About this time she began to have profound hysterical attacks. The atrophy was now increasing rapidly. She had difficulty in maintaining the poise of the head. It tended when unsupported to fall backward or forward. (Fig. 3.) When the occiput approximated the nuchal region she could get the head forward by pushing it with the hands or giving a quick jerking motion forward, which set it up as if it were on a loose hinge. The atrophy of the muscles of the shoulder girdle on both sides was now so advanced that the heads of the humeri dropped from the sockets of the scapulæ, and there was proportionate limitation of movement.

FIG. 3.



Showing position of head when unsupported.

In the spring of 1899 she could still walk with short stride and slow step from one room to another with assistance. Spasticity of the lower extremities now first became considerable. During the entire course of the disease it was never prominent in the lower extremities, but now there was considerable resistance to passive movements, although the upper extremities had become quite powerless, but the bulbar symptoms predominated. The lips were decidedly atrophic. The tongue, which was before irregular and lumpy in its appearance, has become thin and ribbon-like, the seat of incessant vermicular movement. The soft palate, which cannot be raised voluntarily, is scarcely elevated on efforts of intonation, and swallowing is accomplished slowly and with great difficulty. Semisolids are taken most easily. They must be placed on the back of the tongue, then she swallows with great deliberation. Fluids

are regurgitated through the nose sometimes, and attacks of coughing, incidental to some of the food getting into the trachea, are not uncommon. The tendon jerks were all enormously exaggerated, the slightest tap on the patellar tendon sufficed to throw the foot up sharply. The ankle-, elbow-, and jaw-jerks are likewise very much exaggerated. The Babinski reflex was distinctly to be obtained. There were still no sensory, sphincter, or trophic disturbances. Mentally the patient was very much as before, depressed, despairing, and dejected. Threats of suicide were constantly being made. Her reasoning powers were, however, undiminished.

Her emotional state had attracted attention from the beginning. She had no hope, except at rare intervals. Despite her despondency and threats of self-destruction, she was quite sound mentally. The attacks which she began to have about a year before death, and which I have called hysterical, were ushered in with palpitation, tachycardia, and dyspnœa, followed by screaming and violence, as if an expression of agony; stiffness, opisthotonos, unconsciousness, which graduated into sleep, out of which she awakened limp and exhausted. Such an attack would last several hours if not cut short by chloroform inhalation.

A description of one of these attacks, taken from the notes of her case, is as follows: "She becomes frightened, anxious, fearful, tremulous, complains of a feeling of suffocation and of great weight on the chest, and clamors for air. She moans, cries out, thrashes about, and gasps for breath, the respiratory acts being very rapid and labored. Some of the movements that she makes in these attacks are astonishing; for instance, she was lying flat, and with what seemed to be one supreme effort she raised her head and body and bent forward until her forehead struck the bed at her knees, and then she went back again, like the rebound of a ball, to the pillow. She had been unable to raise her head without the assistance of the hands for some time. The pulse in these attacks becomes so weak and feeble that it is scarcely countable. She is sleepless, restless, cast down, wants to die, but is continually clamoring to get well, and cannot be reassured.

The patient died May 25, 1899, after a paroxysm similar to that above described.

The autopsy was performed about four hours after death. Great difficulty was encountered in obtaining a post-mortem examination, and only the brain and spinal cord were examined. The autopsy notes are as follows:

The hair of the scalp is coarse and extremely sparse. The pupils are equal and dilated. The tongue is small, thin, and pale. The skin is smooth, and there were no abrasions. The weight of the entire body is forty-eight pounds. There is extreme atrophy of the muscles of the hands, forearms, and upper arms, and complete atrophy of the shoulder girdles. Some rigidity of the lower extremities. The muscles of the back and of the legs are very small but firm.

The brain was easily removed. It was of average size, and, aside from slightly increased consistency, it was normal macroscopically. The meninges were anæmic and apparently normal. The spinal cord to the naked eye presented a normal appearance aside from the increased consistency in the fourth cervical segment, to be described later.

The cord was carefully segmented, and each segment divided into three pieces for alcohol, Marchi and Müller hardening. Thus prepa-

rations of Nissl, Marchi, Weigert, and picric acid fuchsin were obtained from each segment. Of the lower portion of the cord alternate segments were placed in various fixation fluids.

The oblongata was hardened in formaldehyde alcohol, and the brain in Lang's fluids. I am indebted to Dr. Carlin Philips, instructor of neurology in my clinic, for preparing the specimens—a very considerable task, painstakingly done.

In describing the histopathological changes I shall present briefly the picture of a few of the segments in series.

Second cervical segment, Weigert stain: The neuraxons constituting the columns are normal, with the exception of two symmetrical degenerated areas, as follows: A concentric zone encircling each anterior horn, beginning at the base of the anterior median fissure between the direct pyramidal tracts and the mesial border of the anterior horn, thence encircling the apex of the horn and extending nearly to the peripheral margin of the cord. (Fig. 4.) Thus the tracts involved in

FIG. 4.



Second cervical segment, showing the extent of degeneration in the white substance.

the degeneration are the antero-mesial and antero-lateral of the fundamental columns. Gowers' column, the direct pyramidal tract, and a thin marginal zone skirting the ventral periphery of the cord, are left intact. Although the degeneration spares the ventral marginal zone and the columns of Gowers, it is nevertheless possible that some neuraxons in both tracts may be involved. Scattered through the entire anterior and antero-lateral fundamental columns are many fibres which are normal in every respect. In sections stained with picric acid fuchsin one sees that the neuroglia proliferation is but slight in the areas that show such distinct degeneration with Weigert's stain. In one anterior cornua the motor cells, with the exception of two, have entirely disappeared, while on the other six are to be seen. The smaller cells of the lateral horn appear normal in number and structure.

In the third cervical segment the cornet-shaped area of degeneration is seen to extend dorsally to a greater extent in the lateral columns. (Fig. 5.) The absence of the motor cells is striking, the average number being about two in one anterior horn and four in the other. This

great loss of anterior horn cells, from the upper portion of the second cervical to the lower portion of the third cervical, probably amounts to 90 per cent., and corresponds very well to the loss of function of the deep muscles of the neck. The small elongated cells of the intermediate zone appear to be normal in every way.

FIG. 5.



Outline drawing of the third cervical segment, showing extent of degeneration in the white substance.

In the fourth cervical segment the first striking change in contour and volume of the cord as a whole appears. (Fig. 6.) The deformity in outline is present in the following four or five segments below. It consists of an alteration of contour caused by a sinking in of the

FIG. 6.



Fifth cervical segment, showing change in the contour and volume of the cord, scarcity of cells in the anterior horns (the cells are represented by circles), and degeneration in the white substance. (Composite drawing. Weigert stain for degeneration, carmine for the cells.)

periphery at the point of emergence of the anterior roots. In fact, the periphery of the cord from a point corresponding to the apex of the anterior horn to the lateral tip assumes a concave instead of a convex line. Obviously the retraction of the ventro-lateral periphery of

the cord on either side of the anterior median fissure is due to the contraction of neuroglia growing in the degenerated area described. Inasmuch as this deformity of the cord's contour is not present in the second and third cervical segments, we may assume that the neuroglia in these two segments is of more recent origin than that in the fourth segment.

The area of the degeneration shows some further variation from the previous segments on account of change of shape of the ventral horns of gray matter, the gray matter of the fourth cervical segments extending laterally so as to thrust the lateral horn toward the periphery. The degenerated area from here on thus assumes a sickle shape. (Fig. 7.)

Another respect in which this segment differs from those above is in the degeneration of the marginal zone just ventral to the mesial and lateral boundary of the anterior horn. Aside from these degenerative changes in certain areas as described, the remainder of the white substance appears to be normal.

FIG. 7.



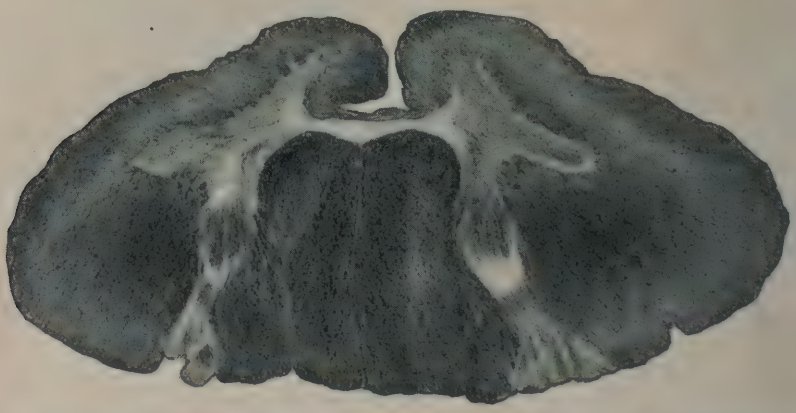
Sixth cervical segment, showing sickle-shaped area of degeneration.

Sections from this level stained by the Nissl method show only three or four large motor cells in each ventral horn. This is an extraordinary decrease in the number of cells, as in the normal cord one can count fifteen to twenty-five. The number of medium-sized and small cells in the region of the gray commissure is not so greatly reduced. In contrast to the findings in other levels of the cord, the lateral horn group at this level is entirely absent. As regards the histological process which caused the disappearance of these cells, the serial phases of it are difficult to formulate, for the reason that the cells that are present are fairly normal. While it is obvious that thousands of cells have disappeared, it is nevertheless difficult to find a single cell body which is actually going to pieces or which shows unmistakable evidences of disintegration. The question is, "How do they disappear?" We find no particular evidence of their destruction, and yet with even a low-power inspection the most striking feature of the whole case is the absence of these cells without a trace of their existence. The remaining cells usually show some confluence of chromophilic plaques into a homo-

geneous mass and yellowish pigment granules which are crowded off into one pole or extremity of the cell. But between this condition of the cell and its ultimate disappearance no intermediate phases can be found.

A brief summary of the findings in Nissl preparations may be made as follows:

FIG. 9.



Weigert stain of the eighth cervical segment, showing deformity of the anterior horns.

1. A fair proportion of the anterior horn cells that have escaped destruction show no great departure from the normal except fogginess and indistinctness of outline of the chromatic plaques.

2. Other cells show confluence of plaques and have masses of yellowish pigment in the protoplasm. The cells of this second class apparently are atrophic. These are illustrated in Fig. 8.

FIG. 10.

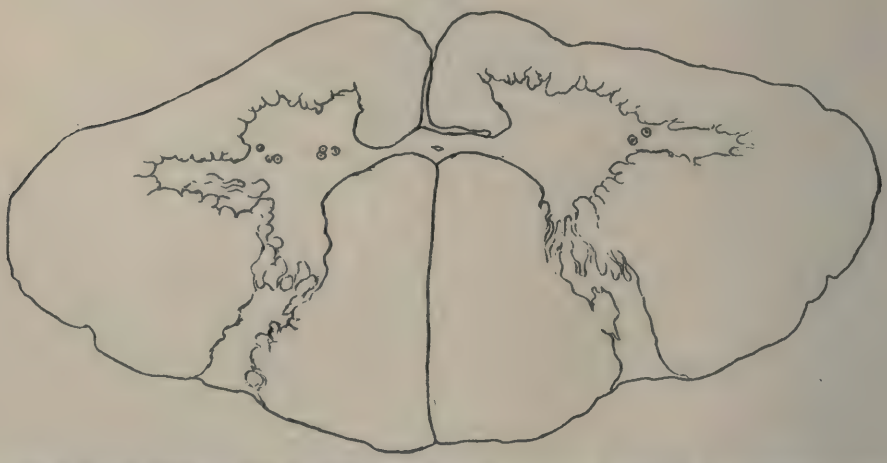
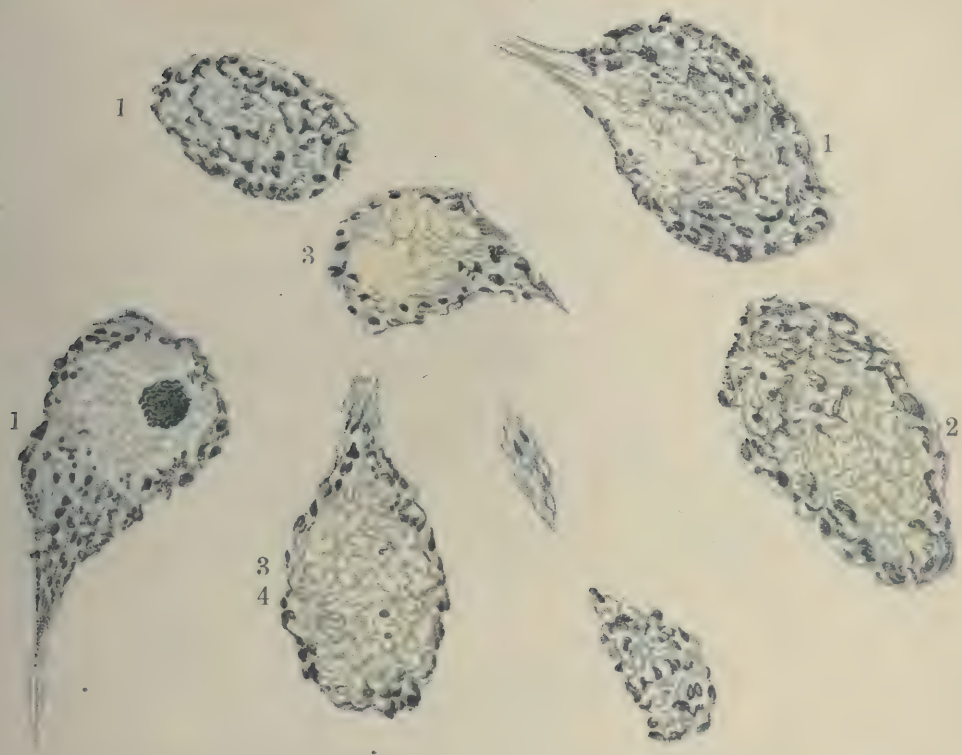


Diagram of the seventh cervical segment, to show paucity of cells in the anterior horns.

Fifth cervical segment practically the same as the fourth cervical.

Sixth cervical segment. In this segment the degeneration extends dorsally in a symmetrical way, forming a tongue-shaped area between the crossed pyramidal and the direct cerebellar tracts, reaching to the end of the posterior horn. The anterior horns are more flattened than in their normal condition, and lie nearer to the ventral periphery

FIG. 8.



Cells of the anterior horns, showing indistinctness of outline (1, 1, 1) of chromatic plaques; masses of yellow pigment (2); plasmolysis (3, 3); chromatolysis (4).

of the cord. The large motor cells of this segment as seen in Nissl preparations show some diminution in number, corresponding proportionately to those observed in the preceding segment; also, the lateral horn group of cells has disappeared.

In the seventh and eighth cervical segments the area of degeneration of white fibres has the same relative distribution, except that it reaches

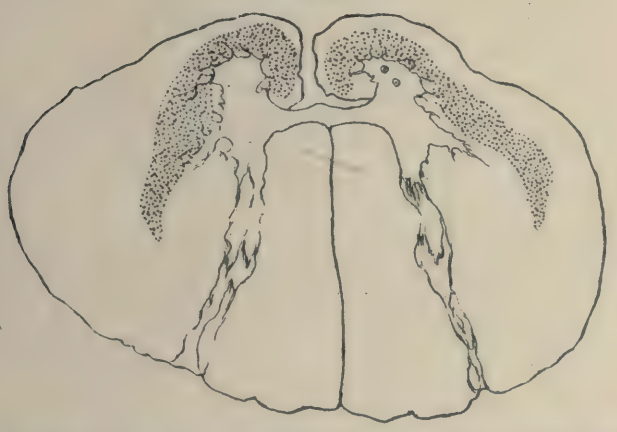
FIG. 11.



To show the area of degeneration in the white matter at the eighth cervical segment.

further inward toward the lateral horn. The anterior roots show marked degeneration when examined by Weigert's method. (Fig. 9.) The cells of the anterior horn are very few (Fig. 10), and are degenerated as well as the groups of cells in the lateral horns. (Fig. 11.) The direct cerebellar tract in this segment shows a few degenerated fibres.

FIG. 12.

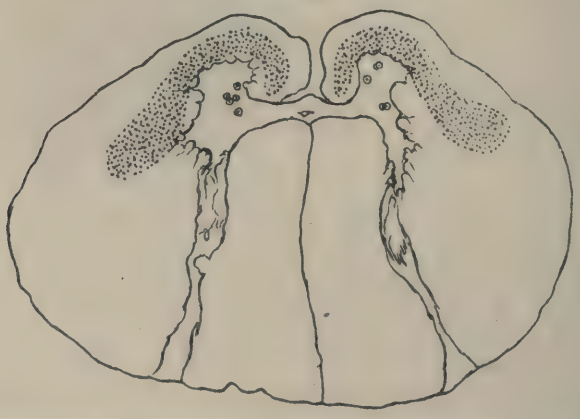


First dorsal segment, to show the progressive diminution of the area of degeneration in the white matter.

From the level of the first dorsal to the fourth, inclusive, the type of fibre degeneration takes the form shown in the upper cervical region, namely, a zone encircling the anterior horns, becoming progressively smaller and less and less intense, until at the level of the fourth dorsal it is scarcely discernible, except for a slight and ill-defined pallor encircling the apex of the ventral horns. (Figs. 12, 13, and 14.)

The disappearance of the motor cells is somewhat more difficult to determine throughout these first four dorsal segments than in the cervical segments, since normally there are so few cells in the ventral horns. There can be little doubt, however, that the atrophy of the cells is present in these segments in about the same proportion as in the cervical cord. The lateral horn cells and those of Clarke's column appear to be normal in these segments.

FIG. 13.



Second dorsal segment, to show the progressive diminution of the area of degeneration in the white matter.

From the fifth to the eleventh dorsal segments the degeneration of the fundamental columns is so slight that it is hardly apparent in sections stained by Weigert's method, yet in picric acid fuchsin specimens there is seen to be present an increase in neuroglia tissue. This confirms the idea that the same degeneration exists, but to a less extent, throughout the entire dorsal region.

FIG. 14.



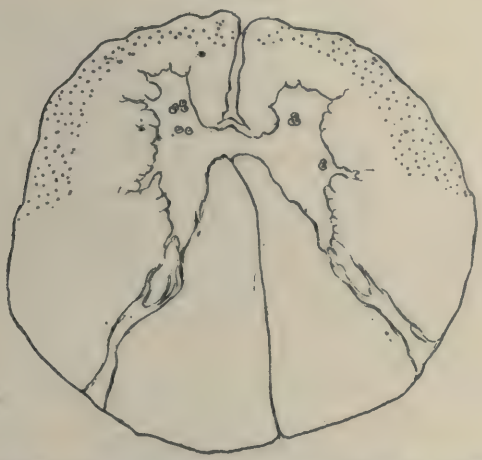
Third dorsal segment. Stippled area corresponds to the degeneration.

What has been said regarding the condition of the motor cells of the upper dorsal also applies to segments of the lower dorsal region. The cells of the lateral horn are normal, while here and there in Clarke's column are groups of cells which are atrophic and are pigmented, with excentric nuclei.

From the twelfth dorsal to the third sacral, inclusive, the zone of degeneration in the ventral half of the spinal cord assumes a radically

different position from that found in other regions. (Fig. 15.) It occupies the peripheral lamina of the ventral half of the cord extending from the lips of the anterior fissure around to a point opposite the apex of the lateral horn, where it expands to a triangular mass indenting deeply inward the region of the cord just ventral to the crossed pyram-

FIG. 15.



To show the degenerated area approaching the periphery.

idal tracts. It may be briefly described as a comma-shaped area, the head of the comma lying against the ventro-lateral border of the crossed pyramidal tracts, and the attenuated tail of the comma extending thence around the periphery of the cord nearly to the lips of the anterior median fissure. (Fig. 16.)

FIG. 16.



Showing the area of degeneration in the lumbar cord.

Relatively speaking, the anterior horn cells throughout the lumbar and sacral regions of the cord are as much diminished in number as in the cervical region. Because the lower extremities were active long after the involvement of the upper ones, we had expected that the lumbar and sacral regions of the cord would show a corresponding

immunity from disease of the anterior horn cells, but such is not the case. I was again disappointed in not finding stages of cell atrophy which would enable me to determine the actual process of dissolution of the cells. Here, as elsewhere in the cord, the cell is either fairly normal in appearance or it has completely disappeared. Throughout the cord the bloodvessels seen are normal.

In the medulla oblongata, from the sections taken at the lower one-fourth of the hypoglossal nucleus, one cannot say that there is any striking loss of the cells. Certainly there is no such loss in this nucleus to correspond with the striking loss of motor cells of the cord. There are, however, positive signs of structural changes, although these are limited to a small proportion of all the cells. Those affected show eccentricity of the nuclei, homogeneous conversion of the chromophilic plaques, or a filling up with pigment granules. I am unable to record any signs of cell disintegration, such as shrinkage or distortion of the cell body. These same anatomical findings are present in the nucleus ambiguus. From the scattered and isolated distribution of this nucleus it is quite impossible to say that degeneration of it exists in a given instance unless it is practically destroyed. Such is not the condition in this case.

The dorsal vagus nucleus is apparently normal. In Weigert preparation of the oblongata from this region the posterior longitudinal bundle is seen to be slightly but distinctly degenerated. This is what we might expect from its relation to the anterior and lateral ground bundle of the cord. Aside from these changes the oblongata was normal. The internal capsule and the corpus callosum were not examined.

Pieces of the motor cortex hardened in Lang's fluids were examined. The large motor cells from the paracentral lobule and from the Rolandic area show a pallor which at first seems to be indicative of structural change. It appears that this change is not confined to these cells, but affects uniformly all the cells of the cortex. These cells are quite as numerous as normal, so having used such an unsatisfactory reagent as Lang's mercuric hardening fluid we concluded that the change is an artefact rather than a true structural change. No statement can, therefore, be made as to the presence or absence of pathological changes in the brain.

The pathological findings of this case may be summarized as follows:

1. Uniform disappearance of the ventral horn cells throughout the entire cord, affecting (possibly) the dorsal region less severely than the cord enlargements.
2. Degeneration of a zone in the anterior fundamental columns skirting and encircling the ventral horns in the cervical and upper dorsal regions, also the anterior portion of the lateral limiting layers. (Bechterew.)
3. Degeneration of a marginal strip of the ventral periphery of the cord expanding dorsally against the ventral and lateral border of the crossed pyramidal tract, and appearing with a comma-shaped head in the lumbar and sacral regions.
4. Deformity of the ventral face of the cord in the cervical and upper dorsal region due to a concave sinking-in of the periphery.
5. Neuroglia proliferation in the degenerative area of white matter, and also in the anterior horns of the cord enlargements.
6. Evidence that the neuroglia proliferation is older in the cervical region. The degeneration is denser in the region and has caused shrinkage of the ventral face of the cord at the emergence of the roots.

7. Atrophy of the anterior roots.
8. Distinct evidence of cell degeneration (chromatolysis, plasmolysis, and disintegration) in the hypoglossal nucleus and the nucleus ambiguus.
9. The pyramidal tracts are intact.

Amyotrophic lateral sclerosis is a disease characterized by the symptoms of progressive muscular atrophy of the Aran-Duchenne type, complicated with bulbar involvement, plus spastic paresis, particularly of the lower extremities, and exaggeration of the tendon jerks all over the body. The morbid process upon which it is dependent consists in a decay of the peripheral motor neurons in the ventral horns, the terminal arborizations of the central motor neuron (in other words, the ending of the neuraxons that come down through the cord as pyramidal tracts), and of the pyramidal tracts themselves, and atrophy of the column (strange cordonal) and commissural cells of the gray matter. The degeneration extends centrifugally in the peripheral motor neurons, centrifugally and centripetally in the central motor neurons. This constitutes when the process is complete a characteristic microscopic picture, the principal features of which are (1) atrophy of the anterior horns and diminution or disappearance of all its cell constituents without noteworthy change in the bloodvessels; (2) degeneration of the fundamental tracts of greater or lesser extent; and (3) degeneration of the pyramidal tracts which may be so slight as to be scarcely detectable, or so complete that it may be traced to the origin of these tracts in the motor cortex. The question whether the peripheral motor neuron—*i. e.*, the root cells of the anterior horns, or the central motor neurons—the pyramidal tracts—are the first to be involved, cannot yet be answered.

Neurologists are well aware that there is much difference of opinion as to the starting-point of the disease. Charcot and the Parisian school generally, with the exception of Brissaud, maintain that the lesion is primarily and predominantly (at least in the beginning) of the central motor neurons, the pyramidal tracts in the spinal cord being diseased first, and that the affection of the white matter is consecutive or "deuteropathic." Brissaud's idea seems to be that the primary seat of the disease is in what Marie calls the supplementary zone, an area ventral to the pyramidal tracts and dorsal to the intermedullary anterior roots made up of the prolongations of column cells in the gray matter uniting different levels of the cord. The pyramidal fibres are involved later, and, finally, the ventral horn cells. This, however, presupposes the secondary involvement of the gray matter, which is the question in point. Dejerine and Thomas, commenting upon this view, say that this opinion of Brissaud is invalidated by the facts. The fact that the lesion of the motor cord is not strictly confined to the pyramidal tracts, but invades the antero-lateral, speaks in favor of Charcot's view. They then proceed to say that the degeneration of the pyramidal tract in

amyotrophic lateral sclerosis is for them indisputable, because they have always found it. This is a denial of the validity of the work of others as well as an expression of finality that few scientific men permit themselves.

Leyden was the first to contest this teaching of Charcot, and he has unswervingly maintained his position. His view is that the peripheral motor neuron is first and predominantly affected, and that the changes in the white matter are sequential. This view is shared, in a measure at least, by many of his countrymen. Gowers teaches practically a similar doctrine, namely, that amyotrophic lateral sclerosis is a variety of progressive muscular atrophy in which the pyramidal tracts are more profoundly affected than they are in the ordinary form of spinal progressive muscular atrophy. This is the view held by many neurologists in this country, for instance, Dana and Sachs.

As a matter of fact, it is impossible to say dogmatically, from histological study of our cases, whether the peripheral or the central neuron is affected first. The truth is probably that in one case the central neuron is diseased first, and in the other the peripheral. When the central neuron is affected first it is likely that the degenerative process begins in the central convolutions and not in the cord. This involvement of the cell body of the central motor neurons causes decay of the entire neuron, beginning in the most remote part—that is, in the spinal cord, the pyramidal tracts, the intercalary neurons, and the terminal ramifications around the anterior horn cells. The fact that the degeneration of the pyramidal tracts progresses upward does not speak against the primary cortical involvement; in fact, it speaks rather in favor of it.

It seems to me that we must admit, because of such a case as the one published herewith, that the lesion in some cases of amyotrophic lateral sclerosis begins in the cells of the anterior horn, and that destruction of the cells therein situated causes the phenomena (in part at least) of the disease, and accounts for the pathological findings. The cells of the anterior horns are of three distinct varieties. First, those which give rise to the anterior roots of the spinal nerve (root cells); second, those that send their prolongations from one side of the cord to the other (commissural cells); and, three, column (cordonal) cells—cells whose prolongations bind one segment of the cord to another by means of so-called association fibres. It is the degeneration of these column cells that causes the area of degeneration in the white matter of the cord in our case. Decay of other fibres, such, for instance, as the fibres of the column of Gowers, was probably incidental to the destruction of these short fibres. It is well known that column cells are to be distinguished from root cells not only by their histological peculiarities, but by their location. They are particularly numerous in the enlargements of the cord, and they occupy a region in the middle of the anterior horn close

to its junction with the posterior horn ventral to the column of Clarke, and to the column of cells described by Onuf and myself in the cat, which we called the paracentral column. The adjacency of these cells to the column of Clarke accounts for the existence of changes in the direct cerebellar tract in some cases which have been described, the lesion of the column cells implicating by contiguity some of the cells of Clarke's columns.

Destruction of these cordonal or column cells causes the degeneration of the fundamental columns in cases of amyotrophic lateral sclerosis and progressive muscular atrophy of the Aran-Duchenne type. That such degeneration does not occur in every case of either one of these diseases in no way invalidates what has been said. In the majority of cases of spinal progressive muscular atrophy such degeneration does not occur, and the explanation is that in such cases the destructive lesion in the spinal cord confines itself to the root cell (*i. e.*, to the ventral portion of the anterior horns), and that the column cells are not implicated. When they become implicated the supplementary zone in the gray matter is found diseased, as was the case in some observations of J. B. Charcot. It is not unlikely that this explanation suffices for all the cases of progressive muscular atrophy with changes in the white matter.

As to the explanation of the spasticity and exaggerated reflexes in a case like ours or that of Wolff, it must be sought for in some alteration to the central motor neuron in the brain which has not as yet extended to such a degree as to cause discernible alteration of its prolongation in the spinal cord.

What has been said should not be construed to mean that the lesion of amyotrophic lateral sclerosis is not often, perhaps always, if the disease lasts long enough, a degeneration of both systems of neurons throughout their entire course. That this is so there cannot be the shadow of a doubt. There are now eleven cases on record (the two cases of Kojewnoff, two of Charcot and Marie, one each of Lennmalm, Lumbroso, Nonne, Strümpell, Mott, Hoche, Spiller, Czyhlarz and Marburg) in which the pathological process involved both systems of neurons in their entirety. My contention is merely that such involvement is not necessary for the existence of the disease clinically. It may exist in its most typical form without any involvement of the pyramidal tracts whatsoever. This is shown by the cases of Wolff and Senator and by my own case. The case reported by Senator and by Wolff was clinically a fairly typical case of amyotrophic lateral sclerosis, especially in the latter stages. On microscopic examination of the specimens there were found atrophy of the anterior horn cells, arterial and venous hyperæmia, multiple punctate hemorrhages, apparently of recent origin, and incipient syringomyelia in the lumbar cord. The changes in the motor spinal cells explain the atrophy in this case, but there is no adequate

explanation of the spasticity. Dercum and Spiller, in commenting upon this case, inquire if they may not venture to suggest that the foci of softening around the hemorrhages had something to do with causing the spasticity. But Wolff has already considered this. In the first place, the softening was almost exclusively of the gray substance around the junction of the anterior and posterior horns, and of the posterior roots. That it could not have been due to the hemorrhages is shown by their recent occurrence. To explain the spasticity it may be fair to assume some involvement of the central motor neurons in the cortex which has not yet gone on to decay sufficient to produce degeneration at their termini. That spasticity may be caused by cerebral lesion without degeneration of the pyramidal tracts is well known. It occurs sometimes with hydrocephalus and with brain tumor, such as in a case diagnosticated as lateral sclerosis, recorded by Schultz, in which the autopsy showed only internal hydrocephalus. There was no trace of spinal-cord degeneration.

When the disease process of amyotrophic lateral sclerosis has reached its completion there can be no doubt, I think, that both motor neurons and the nerve elements which unite the motor nuclei of different levels together are involved, and this constitutes the typical lesion of the disease. Our case may be looked upon as one which stands midway between the cases in which the pyramidal tracts are pronouncedly affected and the case reported by Wolff. For a long time it was doubted that primary sclerosis existed as a pathological entity, although it had long been recognized clinically. The cases of Minkowski (*Deutsches Archiv f. klinische Medicin*, vol. xxxiv. p. 24) and of Dejerine and Sottas came near to fulfilling the requirements, but it was not until Strümpell, Donaggio (*Rivista Sperimentale di Freniatria*, 1897, vol. xxxiii.), and Kuhn (*Deutsche Zeitschrift f. Nervenheilkunde*, vol. xxxii. p. 144) published their cases that there was full substantiation of the existence of this condition. Primary lateral sclerosis must be a very rare disease, but not many years since the diagnosis of lateral sclerosis was not an uncommon one. Now it is rarely made. Careful following up of the cases in which such diagnosis was made has shown that they prove to be examples either of amyotrophic lateral sclerosis or multiple sclerosis; more the former than the latter. Moreover, since the establishment by Erb of the disease known as syphilitic spinal paralysis, some of the cases formerly diagnosticated as lateral sclerosis have found their proper classification there.

The changes in the spinal cord in amyotrophic lateral sclerosis are by no means confined to the anterior horns and the pyramidal tracts. The posterior columns, especially the columns of Goll, have been found diseased a number of times. For instance, the cases reported by Oppenheim, Charcot and Marie, Hektoen, Brissaud, Dercum and Spiller,

Luce, Dejerine, and Sottas. What the significance of these degenerations in the posterior columns is it is not possible to say. It may be that tabes has been superimposed upon amyotrophic lateral sclerosis, or *vice versa*, such as in a case of progressive muscular atrophy plus tabes about to be reported by me. It may be that the neuroglia overgrowth in the cord chokes off some of the fibres making up the columns of Goll, or it may be, as Marie suggests, that the cells of the gray matter that send their axis-cylinders into the posterior columns may be diseased, and thus cause decay of their prolongations.

The direct cerebellar tracts have occasionally also been found implicated by the morbid process. Stadelman was one of the first to call attention to the fact that degeneration of the lateral columns extends in some instances far beyond the confines of the pyramidal tracts, and this has been corroborated by many other observers, particularly by Marie, by Raymond and Ricklin, Spiller, Schlesinger, and others. Oppenheim gave what is probably the correct interpretation of this degeneration of the supplementary zone—*i. e.*, that it is due mainly to atrophy of short fibres uniting segments of the cord to one another.

That amyotrophic lateral sclerosis is a different disease from progressive muscular atrophy of the Aran-Duchenne type must be admitted, I think, also because of its very different clinical delineation. It is difficult to conceive of two diseases whose clinical course is more unlike. Progressive muscular atrophy of the Aran-Duchenne type is slow in its course, oftentimes lasting from five to fifteen years. Amyotrophic lateral sclerosis rarely lasts more than from two to three years. Of course, there are cases, such as that of Dejerine and Thomas, which last much longer, but these are exceptional. A patient with muscular atrophy does not seem to be ill for a long time after the onset of the disease, while in amyotrophic lateral sclerosis he is ill from the very beginning. In the latter there are no periods of cessation of progress or remission, such as there is not infrequently in spinal progressive muscular atrophy. And, finally, the different specific clinical features which differentiate the two conditions need not be here enumerated, as they are too well known. But that the two conditions cannot always be differentiated is well shown by an experience of Raymond. The twelfth lecture in the fourth series of his *Clinique des Maladies du Systeme Nerveux* is devoted to a case of progressive muscular atrophy of the Aran-Duchenne type. Under diagnosis the author says: "Il s'agit indubitablement d'un cas d'atrophie musculaire progressive." The autopsy showed (report published with the series of cases reported to the last International Congress in Paris, 1900, by Phillipe and Guillain) that the lesion was that typical of amyotrophic lateral sclerosis. When the case was examined by Raymond the exaggeration of the reflexes which had previously existed had disappeared.

There are cases of amyotrophic lateral sclerosis in which the spastic symptoms precede the atrophic manifestations, and others in which they predominate. Such cases bespeak an earlier or more profound involvement of the lateral columns than of the gray matter. Moreover, there are trustworthy records of many cases in which the degeneration of the pyramidal tracts was complete, while the process of the disease in the gray matter was still in a state of progression.

It is not easy to understand why there should be so much and such acrimonious discussion as to whether the gray matter or the white is first to be involved. In amyotrophic lateral sclerosis we are dealing with a poison or noxious influence which is capable of causing destruction of two distinct portions of the spinal cord which are rarely diseased simultaneously—the white and the gray matter. If this is admitted, why should not one of them be diseased first in one instance and the other in a second instance?

Whether amyotrophic lateral sclerosis is a part of or a variety of spinal progressive muscular atrophy is another question, and a question which, as I have indicated above, must, it seems to me, be answered in the negative. Although spinal progressive muscular atrophy may be accompanied by disease of the white fibres of the cord which on microscopic examination reveals itself as a degeneration of the supplementary zone, there is never any such degeneration of the pyramidal tracts as that ordinarily found in cases of amyotrophic lateral sclerosis. I do not recall that any case has been recorded in which degeneration of the central motor neuron throughout its entire extent existed. So that from a clinical as well as from an anatomical standpoint it seems the identity of these two diseases must be denied. A little later on we shall see that a consideration of the etiology leads to the same conclusion.

The clinical picture of amyotrophic lateral sclerosis is a very constant one, and liable to but slight variation. The symptoms are typified by the case reported in detail in this paper, so that they do not call for repetition here. In looking through the literature of the subject I have been impressed with the frequency with which mental symptoms have been observed. By this I do not mean cases in which the disease has developed in insane persons, such as in the case of Sarbo and of Dornbluth. Amyotrophic lateral sclerosis may develop in an insane person as well as in a person of sound mind. I am inclined to think that it is an error to classify such cases as that reported by Zacher as a typical form of the disease. A man of thirty developed six years after syphilitic infection disturbance of speech, and later the clinical picture of general paresis, which was accompanied with atrophy in the upper extremity. The autopsy, in addition to many other lesions, revealed changes in the crossed pyramidal tracts and slight alteration of the anterior horns. Nor do I think that such cases as the one recently

reported by Jurman as one of amyotrophic lateral sclerosis supervening in a general paretic after a blow on the jaw which caused a fracture should be included with this disease at all. Jurman's patient developed difficulty of swallowing and of speech, inability to put out the tongue, feebleness of the arms and legs, augmentation of the tendon-jerks, clonus of both feet, difficulty in walking, slight diminution of faradic irritability, and forced laughter. I can see nothing in a symptom-complex such as this incompatible with general paresis. Bearing in mind the widespread and extensive decay of neurons which characterizes general paresis, it is far more legitimate to classify such cases under that disease than to try to put them under the rubric of amyotrophic lateral sclerosis.

The mental symptoms of amyotrophic lateral sclerosis that are worthy of mention are suicidal impulse, such as existed in my case, attacks of meaningless laughter and of weeping without direct cause, occurring in an impulsive manner, and evidences of slight dementia. All of these symptoms may well have their foundation in the organic changes that go on in the brain. It is not improbable that the impulsive, uncontrollable emotional display bespeaks an involvement of the motor neurons extending into the thalamus. In a similar way such cerebral manifestations as those reported in a case by Erben, paraphasia and disturbance of speech and intelligence, may be attributed to disease of the cortico-muscular neurons. The point that may be emphasized here is that mental symptoms occur with considerable frequency in this disease and rarely in spinal progressive muscular atrophy.

The Etiology of Amyotrophic Lateral Sclerosis. The etiology of amyotrophic lateral sclerosis is very obscure, practically nothing is known of the real cause of the disease, and I regret that I am unable to contribute anything. Whatever information is to be derived from a study of a considerable number of cases will, however, be here set forth. After careful examination of the entire literature of amyotrophic lateral sclerosis, I have selected the records of ninety-four typical cases and added to them ten of my own cases, five with autopsy and five without, and have made these the basis of a statistical study.[1]

Of the 104 cases 55 were males and 49 females. It will be seen at once that this is at variance with the statements of many previous writers regarding its frequency in the two sexes. The French school particularly are positive in their statement that the disease is much more frequent in females than in males. Probst, who made a careful analysis of 53 cases in 1898, found that the number was evenly distributed between males and females. As my cases are in nowise

[1] Dr. Joseph Frankel has kindly loaned me the histories of three typical cases, which are incorporated.

selected, merely taken from the literature wherever a typical case could be found, the inference is more reliable than from a small number of cases personally observed. For instance, of the last 7 cases that I have seen personally 5 were men and 2 women.

It is generally held (and I have heretofore shared the view) that amyotrophic lateral sclerosis is more frequent between the ages of thirty and forty. In 100 unselected cases 30 patients were between thirty and forty; 29 between forty-five and fifty; 28 between fifty and sixty, and 2 under thirty. This would seem to show that the decade following the forty-fifth year is equally liable to the affliction.

In 26 cases the total duration of the disease was fifty-five years, which makes the average duration a little more than two years. This coincides with my experience. The briefest duration of the disease in cases found in the literature was five months, and this patient was carried off by influenza. In 2 cases, however, the disease seems to have run its course in six months. Record of 4 cases was found in which the disease lasted only nine months. A few cases only lasted upward of five years; the longest on record seems to be ten years.

The part of the body to be first affected was inquired into with considerable interest. Out of 81 cases in which there was specific information on this point the upper extremity was affected first in 39 cases, the lower extremity in 14 cases, and the upper and lower extremity (hemiplegic), or all four extremities, in 11 cases, while the disease came on with bulbar symptoms in 21 cases. In upward of 50 per cent. of all the cases bulbar symptoms appeared within the first year. But in the cases that are ushered in with bulbar symptoms it is not long before atrophy or spasticity or both show themselves in other parts of the body.

Patients are very apt to attribute their symptoms or disease to influence or experience known to be deleterious to their health, such as exposure to the wet or cold. This is the case particularly when the seemingly attributable cause precedes immediately the appearance of the first symptoms. Exposure to cold and wet, overwork, strife, fright, and bodily injuries were enumerated as causative in 28 instances. In many of the cases on our list no attributable cause is given. Bodily injury was said to have preceded the first manifestations of the disease in seven instances; but the relationship of injury is often very remote, as in the following case:

J. E., aged forty-five years, shoemaker, married, born in Russia; dates the beginning of his illness to July, 1897. He attributes it to a fall from a car three months before, which, however, produced no apparent injury. He complains of weakness in the hands and feet and of difficulty in speech. He has had considerable vertigo, headache, and nervousness, and lately difficulty in swallowing and chewing has been noticed. He complains also of a "drawing" sensation in the legs and hands, of a sensation of coldness in the lower half of the abdomen, and

of heat in the upper half of the body, which is also the seat of profound perspiration. In September, 1897, an examination showed typical spastic gait, short, wooden stride, locomotion being accomplished with great difficulty. Fibrillary twitchings of the shoulder girdles are very conspicuous. The patient is unable to close the mouth tightly on account of fibrillary twitching of the face and weakness of the lip muscles. There is no atrophy.

On March 2, 1898, an examination was made, of which the following is a transcript of the notes:

The patient is of medium size, fairly well nourished, except in the localities where muscular atrophy has reduced the volume of the parts. The head inclines somewhat toward the right side, the eyelids are drooping, and the facial expression is immobile. There are no scars on the body, except one in the right popliteal region, the result of an intentional injury in order to avoid military duty. When the patient is raised the upper extremities are flexed at the first interphalangeal joints. The lower extremity is slightly flexed, and there is plantar flexion at the ankle-joints. Fibrillary twitchings are to be seen especially in the right upper extremities, in the muscles of the shoulders, and in the muscles of the mouth, they are present, but to a lesser degree in the muscles of the lower extremity, and here, too, they are more conspicuous on the right side than on the left. The patient is unable to whistle or to blow out the cheeks, and the mouth is characteristically tapir. The tongue is constantly in the state of undulatory movements, and is very much limited in its excursions without and within the mouth. There is considerable spasticity of both upper extremities, and the tendon-jerks are all exaggerated. The atrophy in the upper extremity is most profound in the extensor muscles of the forearms, and the thenar, hypothenar, and interossei muscles. In the lower extremities the thigh muscles on the right side are reduced in volume. Passive movements encounter marked resistance. The knee-jerks are lively, but there is no patellar or ankle clonus. The increase of tendon-jerks in the lower extremities is not proportionate to the profound spasticity. The plantar reflexes are lively. There is no disturbance of sensation or of the sphincters.

Electrical examination gives the following noteworthy information: To faradic and galvanic excitation the muscles at first showed rather increased irritability; this, however, is soon exhausted, and after the current had been applied a few times excitability is lost for a while. The transition is, however, not a sudden one, but it goes slowly from sharp contraction through various stages of vermiform contraction to entire absence of response. The ulnar nerves do not respond to any current.

Some cases of this disease attributed to injury, such as that of Goldberg, are reported so incompletely that neither the existence of amyotrophic lateral sclerosis nor the etiological connection of trauma is clear to the reader. In other cases, such as that reported by Oppenheim, in which the symptoms came on after severe overexertion, there existed symptoms (hyperæsthesia of the left thorax, anæsthesia for temperature, and pain in the right leg) which are never present in typical cases of the disease. On the other hand, there are cases, such as those of Strümpell and others, in which trauma seems to have been the imme-

diate antecedent of the appearance of the disease. Just how trauma acts to disease the motor neurons is not clear. Whether by the depreciation of mental and physical vitality or by the production of metabolic products which act injuriously on the motor neurons to facilitate the occurrence of the disease cannot be said. From a review of all the cases reported it may be said that trauma does not seem to be an adequate cause of the disease. Personally I have never seen a case in which I thought it had the slightest etiological influence. Overwork, and especially overwork of a particular character, such as that of gold-beaters, embroiderers, etc., which calls for exhausting use of certain sets of muscles and which plays a rôle in the etiology of spinal progressive muscular atrophy, does not seem to enter into the etiology of the disease under consideration. It occurs mostly among the working class, but no particular occupation would seem to stand in relation to it.

There is much in the natural history and occurrence of the disease which reminds one of an infectious or intoxication process, and it was with considerable interest that the list of cases that I have selected was looked through to determine if there were any information to be had upon this point.

A number of cases have been reported which developed within a short time after parturition. These may be dependent upon some unknown toxic substance. The following case is an excellent example:

Mrs. P. V., aged thirty-four years, born in Russia, married, and has six children, four of which died in early childhood, two are living and well. She has always had good health. Her present illness began a year ago, immediately after the birth of her last child. She arose the sixth day after a normal labor, and soon experienced an increasing weakness of all of the extremities. Within the next six months this had increased to such an extent that she was unable to get out of a chair or to help herself, as in eating and in dressing, with the upper extremities. There was no complaint of pain or of disturbance of the sphincters. She complains now, December 7, 1895, of a "tension in the nerves" (spannung), and of nervousness, of stiffness of the legs, and of paralysis of the four extremities. Examination at this time shows a woman of medium size, fairly well nourished, lying in bed. She is unable to stand, to sit, to work, or to make any movement except of the head, and limited movements of the upper extremities. The left upper extremity is weaker than the right. There is no difficulty in swallowing, but she says that it requires much effort for her to speak, and her voice is slightly husky. There is pronounced atrophy of the thenar, hypothenar, and interosseous muscles of both hands, more advanced in the right hand. Atrophy of both shoulder girdles, more pronounced on the right than on the left, and distinct fibrillary twitching in the atrophying muscles. The jaw-jerk is very lively, the elbow-jerks are increased, the knee-jerks are somewhat plus, the plantar reflexes are absent. There is no atrophy of the muscles of the lower extremities despite the motor paralysis, but fibrillary twitchings are noted from time to time in the muscles of the thigh. There are no sensory disturbances, the sphincters

are intact. The notes of examination, made six months later, are as follows:

The patient has become more helpless. She now has difficulty in swallowing, food frequently gets into the larynx, and liquids often regurgitate, and there is marked disturbance of speech. It is very difficult for her to speak at all when she is lying flat. Respiration is hurried and shallow, and the accessory muscles of respiration are constantly being called into play. The respiratory murmur is scarcely audible. The atrophy of the upper extremity has become more profound. Passive movement of the left shoulder meets with elastic resistance and is painful to the patient. She is still able to elevate the shoulders slightly and to flex and extend the right arm to a very slight extent. She can also make limited movement of the right toes. The atrophy, which involves the supraspinatus, deltoid, muscles of the forearm, the lumbricales, interossei, thenar, and hypothenar eminences, is very advanced on the right side. There is fibrillary twitching in all of the atrophic muscles. The response to galvanic current is sluggish and vermiform, the best contraction being obtained by the kathode. The galvanic reaction is lost in the peroneals, diminished in the nerves of the upper extremities. The faradic irritability is still present but very sluggish. The tendon-jerks are increased; there is considerable spasticity of the upper extremities, less in the lower extremities. The patient now has attacks of spasmodic crying and laughing.

Six of the patients gave a history of syphilis. This is probably not more than the actual percentage of syphilization. In two of these cases, both my own, there may have been some direct relationship between the syphilitic infection and the amyotrophic lateral sclerosis. A brief outline of these cases is as follows:

The patient, a single man, forty-nine years old; was by occupation a house and sign painter. He has never had lead poisoning. When forty-four years old he contracted syphilis, for which he had no treatment save local application. Two years afterward, without apparent or attributable cause, the muscles of the left hand began to atrophy. A few months later the atrophy began in the left leg, and about the same time he began to be slightly spastistic. The atrophy, which was in active progress at the time of his admission to the hospital, now involved both upper extremities, the left more than the right, and to a slight extent the left lower extremity. The tendon-jerks of the knees, ankles, and elbows are much exaggerated, the left more than the right. There is no ankle clonus. The patient complains of stiffness and a feeling of tension in the back of the neck. There are no sensory or sphincteric disturbances. Bulbar symptoms have not yet shown themselves.

In the second case the syphilitic element in the disease seemed to be of much importance. This case is clinically a typical example of amyotrophic lateral sclerosis. Still, it is not unlikely that the pathological process upon which it is dependent is a syphilitic disease of the spinal cord, syphilitic myelitis, if we wish to use that term, the brunt of the lesion being borne by the anterior horns with coincident or secondary

involvement of the white matter around them. It is probable that the pathological change in such cases begins in the bloodvessels and constitutes a syphilitic arteritis or endarteritis, and that the changes in the parenchyma are secondary.

A plumber's assistant, aged forty-eight years, contracted syphilis when thirty-six and received treatment until the local manifestations of the disease had disappeared, *i. e.*, for two or three months. He remained well until the end of August, 1902, when, while driving nails into a resistant wall, the left hand wielding the hammer, he experienced a sense of increasing powerlessness in the left upper extremity. He had to quit work, and has not returned to it since. The weakness of the left upper extremity continued to increase, and soon became manifest not only in the shoulder but in the forearm and hand, the flexors being particularly weak. Within a month he remarked some weakness of the muscles of the right forearm and hand, the two middle fingers being weakest. About six weeks after the onset of the symptoms he noticed for the first time atrophy of the muscles of the left shoulder girdle, and later of the muscles of the arm and forearm. Aside from the sensation accompanying fibrillary twitching in the atrophying muscles, the patient made no complaint.

Examination three months after the attributed onset of the disease revealed profound atrophy of the muscles of the left shoulder girdle, the biceps and triceps, and slight atrophy of the pectoral muscles. The flexor muscles of the left forearm are more atrophied than the extensors on the left side, while on the right side this condition is reversed. The tendon jerks are very much exaggerated all over the body. Myotatic irritability is slow. The plantar reflexes are very lively and of the flexor type. The abdominal reflexes are present, and the cremasteric diminished. There is some increased resistance to passive movements of the lower extremities. All forms of sensory stimulation are interpreted correctly. The pupils are reduced to a pin-point and dilate very slightly in the dark.

There are a number of cases similar to this recorded. In some of them the diagnosis of subacute poliomyelitis has been made on account of the rapidity with which the symptoms came on, or because of rather sudden accession to the symptoms. The explanation of such abruptness is, I believe, that one or more diseased bloodvessels ruptured and caused rapid destruction of surrounding nerve cells. I would not be understood to say that I consider these cases genuine examples of amyotrophic lateral sclerosis. The point that I wish to make is, that there are cases of syphilitic disease of the cord (best designated at the present time as focal myelitis) which parallel the symptoms of amyotrophic lateral sclerosis, in the beginning at least, very closely, and that these may be called syphilitic amyotrophic lateral sclerosis.

In the first case the patient's occupation may have had something to do with the development of the disease, for there have been cases recorded in which lead poisoning would seem to have had some relationship to the development of the disease, as in the following case :

A house painter, thirty-five years old, of good habits, and who denied syphilitic infection, gave the following history: Four years before the onset of his present symptoms he had a typical attack of painter's colic, from which he recovered in a fortnight, since when he has kept at his work. A year ago he first noticed weakness of the little finger of the right hand. Soon after the atrophy became evident, not only in the hand, but in the right shoulder girdle. The atrophy was accompanied with marked fibrillary twitchings, "cramped" feeling in the arms, and pain and stiffness of the neck. The knee-jerks, ankle-jerks, and the triceps-jerks are exaggerated, and there is an atypical Babinski reflex. Bulbar symptoms have not yet shown themselves.

In a case of this kind it may be a mere coincidence that the disease occurred in a worker with lead. But knowing, as we do, that lead has a special predilection to attack motor neurons, it may well be that it bore some relationship to the immediate development of the disease in this case. In fact, it may be said that all of the factors that have been attributed as in some manner causative of the disease, such as injuries, exposure, intoxications, and the like, act only as the fuse to ignite the pile that is already prepared. Back of it all is the *something* which is the real cause of the disease.

Finally, a great deal has been written about an innate disposition on the part of the neurons to undergo degeneration when subject to influences which would be innocuous to properly endowed and developed neurons, an abiotrophy of the motor neurons, to use a term recently introduced by Gowers. It must be admitted that the tissues are endowed with a certain vital resistance, and when this wanes off they readily fall a victim to injurious influences, but amyotrophic lateral sclerosis has, in the main, the clinical features of an active destructive disease, not a decay. Although I am willing to admit prenatal influences, there must be some more tangible and actively operative cause. It is not unlikely that we must look to the pathological chemist for the discovery of the real noxious agency.

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CONGENITAL DISLOCATION OF THE SHOULDER.

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Congenital dislocation of the shoulder is of infrequent occurrence, and recorded cases of this affection are still very few in number and some of them are of doubtful value. Instances are recorded in adults and it is only on more or less certain commemoratives that the congenital nature of the condition has been diagnosed. Other cases have been met with in the fœtus, but in these a detailed account is wanting.

I have endeavored to collect all reported cases of congenital dislocation of the shoulder, but there are only a few that are really conclusive.

Many of them appear to me simply traumatic dislocations occurring during delivery, and in these cases the condition is usually a separation of the epiphysis, while others are instances of infantile paralysis. Still others are simply a diastasis due to a relaxation of the ligaments; while still others appear to have a distinctly congenital origin, which is proven by an electrical examination of the muscles or by post-mortem examination. In this paper I shall deal only with the two latter conditions.

The history of congenital dislocations goes back to Hippocrates, who speaks of them in several passages of his writings, but since his time the attention of surgeons was nearly turned away from this congenital defect until that great master, Ambroise Paré, again called attention to this type of lesion, although he appears to have had the traumatic obstetrical type more in view, for he says: "Car souventes fois les luxations arrivent aux enfantements difficiles quand les sages-femmes, tirant les bras des enfants, disloquent les iouointures de

l'espaule ou de la cuisse." From this time on little seems to have been written on the subject until William Smith contributed an article in 1839 in the *Dublin Medical Journal*, and again in 1847 in his *Treatise on Fractures*, this author publishes two cases of his own. In 1841 Gaillard published a case of congenital dislocation of the shoulder in the *Mémoires de l'Académie de Médecine*, which, unfortunately, like many others, was not proven by an examination of the periarticular muscles, but which, nevertheless, may be included in the congenital form on account of the deformity of the articular ends, which was easily demonstrated because of the extreme thinness of the tissues of the patient. At about the same time—that is to say, in 1841—J. Guerin considered the question more fully and admitted three varieties of congenital dislocation of the shoulder, namely, (1) directly downward, (2) downward and inward; (3) outward and upward. He quotes several examples upon which he based this division, but only one appears to me as demonstrated, and this was a fœtus presenting a subdislocation of the humerus outward and upward.

A few years later Bouteillier published, in the *Bulletin de la Société Anatomique* of 1849, a case of congenital deformity of the shoulder in a patient afflicted with Pott's disease. At the same time Cruveilhier wrote in his *Traité d'Anatomie Pathologique* the following passage: "Il faut bien se garder de confondre avec les luxations congénitales de l'humérus de simples diastases par relâchment des ligaments, telles que la diastase de l'articulation scapulo-humerale dans le cas de paralysie du deltoide. . . .

"Sur six cas présentés par Smith, il n'y en a que deux qui présentent une double luxation (luxation symétrique); seuls, ces deux cas ont été l'objet de dissection, et peuvent, par conséquent, être pris comme preuve a l'appui.

"Dans les autres cas, on s'est basé: (1) d'apres les commémoratifs, ni les malades ni leurs parents ne se rappelant aucune violence extérieure dirigée contre l'épaule; (2) d'après les signes cliniques fournis par l'examen de l'articulation.

"Voici, d'ailleurs, la description détaillée d'un fait que j'ai eu l'occasion d'observer et que je crois appartenir a une luxation congénitale de l'humérus dans la fosse sous-scapulaire. *Il serait cependant possible qu'il dût être rapporté a une diastase consécutive à une paralysie musculaire.*"

Alphonse Robert wrote a thesis in 1851, entitled *Des vices congenitaux de conformation des articulations*, in which he reviews those cases which had been published on the shoulder-joint and mentions those that have already been alluded to. But the most important contribution to the study of congenital dislocation of the shoulder that had appeared up to that time was a thesis upheld at Paris in 1866 by

Leonidas Loignon, and in this work the author had carefully collected twenty-four cases of dislocation of the shoulder, among which only a small number could be classified as congenital. Meyer reports an interesting case and also states that d'Outrelepont had told him that he had seen a dead-born fœtus at term which had a double dislocation of the shoulder. The labor had been an easy one. A projection of the acromion and an infra-acromial depression were noted, while the head of the humerus was found under the coracoid apophysis. The shoulder and the arm were less developed than on the opposite side.

In 1879 Jenni reported a case of congenital dislocation of the left shoulder, and in the same year Küster recorded an instance of a one-year-old child presenting a congenital backward dislocation of both shoulder-joints. Nothing more appears to have been written on the subject until about 1895, when Phelps commenced to write on the lesion. Another case was reported by Lewis, of Philadelphia, in the *Medical News;* then in 1898 two others were published by Scudder, of Boston, in THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, one by Eve, of London, while the latest contribution that I have been able to find appeared in 1901 in the *New York Medical Journal* from the pen of Dr. Marsten, of New York. I would say, however, that Kirmisson, in his *Traité des Maladies chirurgicales d'origine congénitale*, devotes a short article to dislocations of the shoulder, and after remarking that the affection is of extreme rarity, the greater number of instances being due to a paralysis or to a traumatism inflicted during birth, he admits three varieties, namely, (1) subcoracoid, (2) supra-acromial, and (3) infra-acromial and infra-spinous. He also says that he has met with a congenital infra-acromial dislocation in a girl aged fourteen years; the arm was atrophied and shorter than its fellow, while the movements of the shoulder, more especially that of elevation, were very incomplete.

The etiology and pathogenesis of congenital dislocation of the shoulder-joint are most obscure, and many are the opinions that have been emitted by various authorities, but there is not one that gives entire satisfaction. It is far from my intention to make the pretention of adding a new theory to those already existing, and I simply propose to examine the principal ideas which have already been emitted and discussed regarding the subject of congenital dislocations in general.

Now, in the first place, a point that strikes one's mind most forcibly in the study of the etiology is the greater frequency of congenital dislocation in girls than in boys, and this predilection for the female sex is most difficult to explain. It has been upheld that the skeleton of woman and those of man did not have exactly the same disposition; but, nevertheless, at the beginning of life it appears to me that the same dispositions exist in the same degree in both sexes.

In considering the subject of congenital dislocations of the hip, Roser formulated an hypothesis according to which the testicles are the starting-point of reflexes which prevent the fœtus placing his lower limbs in positions which would be favorable for the displacement of the head of the femur. Although this hypothesis is quite suggestive, it does not explain what cause may prevent unfavorable positions in the other limbs, and particularly the structures composing the shoulder in male infants. It is, nevertheless, a fact, which has been amply demonstrated by Broca, that congenital dislocation of the hip occurs in male children in 80 per cent. of the recorded cases.

Another fact which is interesting, and to which I believe no satisfactory explanation can be given, is that congenital affections are more frequently met with in girls belonging to the lower classes than in those born of well-to-do parents. I think that in the case of congenital dislocations intra-uterine rickets may possibly play a certain rôle.

There is another etiological factor besides the question of sex that is most important to consider, and this is heredity. Geoffroy Saint-Hilaire has said that in all ages it has been known that parents often transmit anomalies of organization with which they may be affected to their descendants, just as they transmit their physical constitution or their moral and intellectual qualities. Sometimes the father or the mother only give this unhappy heritage to the children, either of their sex or of the opposite, while occasionally, on the other hand, they transmit the deformity equally to the children of both sexes, and the ills of one individual thus become the common property of an entire race. Occasionally even a perfectly formed normal subject, but who was the issue of ill-formed parents, will see the anomalies which afflicted the latter reappear in his children.

In order to explain the existence of hereditary deformities a primordial defect in the organization of the germs has been admitted, and these congenital defects, according to this theory, are due to an aberration in the formative force—in other words, to a disturbance arising in the process of formation. It often happens that the ends of bones composing a joint have an abnormal form or direction from which a malformation of the joint ensues.

Alcoholism, tuberculosis, and syphilis in the parents or ancestors have often been accused of producing congenital deformities, and from the light that has been thrown on this important subject by modern researches in embryology, it would appear to me that these are potent factors. Other than the two circumstances already mentioned, namely, the much greater frequency in the female sex on the one hand, and heredity on the other, which at the present time are certainly above discussion, absolutely nothing is known regarding the etiology of congenital dislocations.

The pathogenesis of congenital dislocations is a much discussed question, and has given rise to numerous and dissimilar theories. The oldest one, which goes back as far as Hippocrates, considers congenital dislocations as due to an intra-uterine trauma, and although this explanation is far from satisfactory, it has been upheld by J. L. Petit and Cruveilhier. In 1876 Preuss, in considering the etiological part played by trauma occurring to the mother during pregnancy, reported a case of a woman in the fourth month of gestation who fell on a hard object, striking on the left side of the abdomen. She gave birth to a lusty boy, who presented an irreducible dislocation of the humerus and a fracture of the forearm which had united with the formation of a bone callus. This authority at the same time pointed out the bad influence exerted by dress, riding, dancing, and heavy work during pregnancy. But this theory does not explain why the dislocation occurred, and still less why the dislocation is often a double one, and for that matter no anatomical fact can demonstrate the effect of a trauma upon the production of a congenital dislocation.

The second theory which attributes a congenital dislocation to a disease of the joint of the fœtus during intra-uterine life has no foundation whatever. Hypertrophy of the adipose tissues between the articular surfaces, tubercular arthritis, and hydrarthrosis, with a consecutive relaxation of the ligaments, have all in turn been incriminated as factors in the production of congenital dislocation. But the trouble is that these diseases have never been anatomically demonstrated, and Lorenz has said that in opening such joints he has never been able to find an increase in the quantity of the synovial fluid.

In 1890 Pfender endeavored to demonstrate that congenital dislocations were a manifestation of hereditary tuberculosis; but he only succeeded in proving one thing, and that is that tuberculosis is very frequent and that it does not prevent a child from having a congenital dislocation.

Besides traumatism, or any other affection of the fœtus during pregnancy, J. L. Petit, d'Outrelepont, and others, have stated traumatism during labor as a cause; but in point of fact this theory is not acceptable, because not only in several cases the obstetrician was not obliged to interfere; but the researches of Duchenne, Vallette, Lorenz, Krönlein, Loignon, and Hofmokle, regarding traumatic dislocations in the newly born, have demonstrated that according to the anatomical conditions a fracture or a separation of the epiphysis will take place under the action of external violences, such as torsion or traction, but that dislocation never results.

The fourth theory has been advanced by Jules Guérin and Verneuil, who believed that every congenital dislocation was due to a pathological condition of the muscles, resulting from an infantile paralysis. For

both these authorities the cause of the dislocation was a loss of muscular equilibrium; but, contrary to Guérin, Verneuil denied that muscular contracture played any part in the production of these lesions.

From the cases reported in the literature including my own, I think that it is easily proven that a congenital dislocation may occur without any symptom of infantile paralysis being present, and in my own case, as well as from one recorded by Picot, it will be observed that all the electric tests were preserved in all the muscles surrounding the shoulder-joint, and, consequently, all possibility of a myelitis could be eliminated.

The last theory, which is due to von Ammon—the so-called theory of arrested development—remains to be briefly considered. This authority includes this malformation among the congenital articular dystrophies. This theory, however, has undergone many changes from those who have studied it. There are some who believe that a congenital dislocation is due to an absolute absence of parallelism in the development of the joint cavity and the head of the bone which it is intended to receive. In other words, this simply means a disproportion between the container and the contained.

Other authorities recognize the fact that in reality the lesions are far more complicated, and that they not only occur in the joint cavity, but on the articular extremity of the bone as well, so that all the elements entering into the formation of the joint participate in the deformity.

This latter theory is perhaps the most acceptable, and explains why heredity may be one of the most important etiological factors in the production of these deformities; but, nevertheless, it must be said that the study of etiology and the pathogenesis of congenital dislocations has not made much progress since the time of the writings of the great physician of Cos, and still remains a most obscure question.

The pathological lesions found in congenital dislocation of the shoulder are pretty much the same in all the recorded cases, and what is most striking is the arrest in development of that portion of the skeleton upon which the muscles take their insertions. The muscles, too, are atrophied. The capsule of the joint is intact, and its insertions are normal. It is only somewhat relaxed, very distended, and occasionally considerably elongated.

If we consider those cases which have been examined necroscopically, it will be noticed that an arrest in the development of the bones forming the shoulder-joint is noted in all. In Bouteillier's case the shoulder was badly formed, the articular cavity was almost filled up and its cartilage was wanting; the humerus was slender and inflected, while its head was flattened.

In both cases recorded by Smith the glenoid cavity was reduced to

about one-third its normal size, while its internal border was completely wanting; the humerus was thin and atrophied, while its head had an oval shape, the largest diameter being vertical. In Mayer's case the glenoid cavity had completely disappeard, while the head of the humerus, which was oval or rather oblong in shape, was in direct contact with a newly formed cavity which had been produced from the border of the glenoid.

Cruveilhier found a glenoid cavity and apophysis forming a flattened stump, deprived of cartilage and directed outward; the head of the humerus was greatly deformed, and the small trochanter projected markedly. In all cases the capsule was found intact and presented its normal insertions on the bone. In my own case and that of Bouteillier it was very much distended.

In most cases the muscles were found generally atrophied, but this atrophy was due to a decrease in the number of fasciculi, and consequently was a true atrophy due to a formative defect and not from degeneration. It is the same arrest of development as is found in the extremities of the bones, and from this it results that certain muscles are shortened while others are elongated, according to the new position that the head of the humerus occupies in the articulation.

For the same reason the bloodvessels and the nerves may be altered and shortened; but although this shortening is of no great consequence for the bloodvessels on account of their elasticity, it has its importance for the nerves, whose functions might be badly disturbed if brutal manœuvres in the reduction of the dislocation were undertaken.

When we are dealing with a malformation of the shoulder-joint, we should consider two things: First, the recognition of the congenital nature of the disease, and, second, if such be the case, the structures entering into the formation of the joint should be carefully examined. The congenital nature of the affection is not always an easy matter to decide, because oftentimes the diagnosis can only be based on the commemoratives of the parents. The general aspect of the deformed shoulder rarely indicates the affection with which one is dealing, and for this reason the question of heredity and personal antecedents of the patient should never be neglected.

It is quite natural that if in the ascendants of the patient several of them are found to have had similar conditions, or if in the patient two or more malformations are also present, it is most probable that the condition is a congenital one.

Many errors have been committed, and I would mention as instructive one that was made by Nélaton in a case diagnosed as a congenital dislocation of the shoulder. The patient died and at the necropsy lesions of the circumflex nerve and the cervical portion of the cord were found.

The principal character which will allow one to distinguish a congenital origin from an accidental affection may be stated as follows, namely, that a congenital dislocation is usually easy to reduce, but very difficult to maintain reduced; while in the case of an acquired dislocation reduction is almost always impossible, but if it can be accomplished the parts are easily retained in place. In Picot's case all that was necessary was to seize the left arm and give it a slight rotation outward, and the head of the humerus was reduced without difficulty; but as soon as the arm was liberated, the head of the bone immediately returned to its former position. Jenni treated his case by a prolonged extension with rotation, and the dislocation recurred ten times. In my own case reduction could be partially accomplished under ether, but the parts would not remain in place.

Continuing the question of diagnosis, I would point out that two circumstances must be distinguished, the first being relative to the length of time after birth that the subject is examined, whether it be at the time of birth or a few days afterward, or when the child has attained several years or more.

If we examine a child at the time of birth or within a few days following, we may be simply dealing with an intra-uterine traumatism, in which case the commemoratives will be of great assistance. The etiological action of intra-uterine traumatism is not absolutely proven, and in the cases that I have collected this accident has not been met with during the pregnancy.

On the other hand, we may be dealing with an obstetrical traumatism. It is well known that a traumatic dislocation during labor is extremely infrequent, and that it is in most instances in reality a fracture of the upper end of the humerus or a separation of the epiphysis. Under these circumstances, besides the absolute impotency of the fractured limb, a painful tumefaction will be found around the joint. The search and manipulation is not an easy thing to carry out in a very small baby, but if gentleness and perseverance be employed, the painful region may be quite exactly mapped out and occasionally a very slight crepitation may be elicited, and there will be found a more or less extensive ecchymosis.

These symptoms are wanting in congenital dislocation of the shoulder, in which case the joint is perfectly free and all symptoms of an inflammatory process are lacking. Congenital dislocation of the shoulder may also be confounded with a congenital relaxation of the articular ligaments; but in this case the dislocation is not present when the limb is in repose, but it is produced with the greatest ease when any slight effort to use the arm is made. After reduction the parts remain in place.

Obstetrical paralysis is characterized by its usual location in the

deltoid, infraspinous, and flexor muscles of the forearm. The arm hangs down in internal rotation and lies against the thorax, while the hand is in pronation and the fingers flexed. Since the deltoid muscle is always involved in root palsy, the shoulder is depressed, immovable, and the arm cannot be raised. Nevertheless, since the trapezius is not involved, this muscle may give a few feeble movements to the shoulder.

Sensibility is completely preserved in the entire extent of the upper limb, but if the electric reactions of the paralyzed muscles be studied, it will be found that they do not respond to the faradic current, or, if they do, it is only faintly. In the beginning, at least, they do react to the galvanic current.

What distinguishes most positively a congenital dislocation of the shoulder from the paralysis is the preservation of the functions of all the muscles of the joint and their distinct excitability to electricity. In my own case, as well as in some others, all these reactions were present, and it is most unfortunate that in the other reported cases this part of the examination has been neglected.

Congenital dislocation of the shoulder may be differentiated from syphilitic pseudo-paralysis, inasmuch as the latter disease hardly ever makes its appearance before the first or second month after birth. It also coincides with more or less advanced lesions of the bones, as well as with cutaneous and mucous manifestations of syphilis, while a dislocation, on the other hand, dates from birth and there is an absence of syphilitic stigmata.

We should also bear in mind the differential diagnosis between dislocation and a paralysis having a cerebral origin; but in the latter condition the paralysis is only exceptionally monoplegic. In most instances it takes on the hemiplegic type and includes both upper and lower limbs and the inferior facial nerve.

In those cases where the child has already attained several years in age, we will, in the first place, be obliged to eliminate all the ordinary lesions which affect the joints. Acute articular rheumatism is characterized by a periarticular swelling, with a more or less acute pain on pressure. Spontaneous pain is also present and is frequently accompanied by fever. In congenital dislocation of the shoulder pain and swelling are absent, but there may be present some faint intra-articular cracklings which possibly might be mistaken for rheumatism. Generally considered, however, the symptoms are too evident to be misleading.

An old tubercular infection of the shoulder resulting in a spontaneous dislocation is a very rare condition, but its existence has been admitted by good authorities. The differential diagnosis is quite difficult, because it occasionally happens that the affection is cured without

leaving any external traces, and that the movements of the dislocated shoulder may in certain cases be quite as limited as those of a joint affected with an old white swelling. The presence of cicatrices resulting from former abscess formation will greatly aid in settling the diagnosis. The difficulties, however, become greater if we are dealing with a tubercular lesion occurring in a congenitally dislocated shoulder, and in this case we can only be guided by the commemoratives relative to the former condition of the joint.

Traumatic dislocations are of an extreme infrequency, and usually such cases are in reality either a fracture of the upper end of the humerus or a separation of the epiphysis. All young children are exposed to these affections, but after the age of two years they become more infrequent, while past the age of ten years they are exceptional. In cases of doubt radioscopy must be resorted to.

Progressive spinal amyotrophy of infancy can be recognized by the fact that it begins during the first year of life, denoting its presence by a paresis with atrophy of the muscles of the thigh and buttocks, and absence of symptoms of infection. It successively reaches the vertebral muscles of the neck and scapula, the arm and the forearm; then the muscles of the leg, the hands and the feet become involved. The progress of the atrophy is progressive, chronic, and symmetrical. Electric excitability is diminished and the reaction of degeneration is always present.

In the juvenile type of progressive muscular atrophy an error in diagnosis of congenital dislocation of the shoulder can hardly be made. Erb's disease appears either during early infancy or in young children, occasionally at puberty. Its commencement is insidious and shows itself as a weakness of certain muscles of the shoulder and arm, which can be detected when certain movements are made. The affection is always accompanied by a more or less apparent loss of flesh.

The muscles that are at first attacked are generally the pectoralis major (excepting in its clavicular portion), the pectoralis minor, the lower fasciculi of the trapezius, the dorsalis major, the rhomboids, the biceps, some of the muscles of the neck, the anterior brachial, and the supinator longus. Some groups of muscles are nearly free from the atrophic process, such as the sternomastoid, the coracobrachial, deltoid, the infraspinous and supraspinous, the muscles of the forearm, excepting the long supinator, and the thenar and hypothenar muscles. Electric excitability is proportionately diminished to the degree of atrophy present, while the reaction of degeneration is not distinct.

Landouzy-Dejerine type of paralysis is chracterized by a paresis and atrophy of the muscles of the face, shoulder, and arm. This myopathy occurs during early infancy and usually begins in the muscles of the face. The projection formed by the deltoid is replaced by a depression

through which a subdislocation of the humerus may be made out. This subdislocation is due to a relaxation occurring in the elements constituting the shoulder-joint. As the disease progresses the pectoralis major, the trapezius, the sternomastoid are each included in the process and undergo atrophy which contrasts very greatly with the normal condition of the muscles of the forearm and the hand.

Infantile spinal paralysis has often been accused of producing dislocation of the shoulder, and some have even gone so far as to deny the possibility of a congenital dislocation of the shoulder, believing that such a lesion was due to infantile paralysis. This disease is more frequently met with in early infancy, although infrequently it may occur later on in life. It begins suddenly with convulsions, cerebral symptoms, and temporary contracture. At the same time a fever, which lasts from one to eight days, makes its appearance, occasionally with remissions.

The disease attacks at once all the muscles that are to be affected. After this regression takes place and certain paralyzed muscles recover their electrical and voluntary contractility, while others remain paralyzed and undergo a progressive atrophy.

A congenital dislocation is noticed immediately after birth, and there is a complete absence of fever. All the muscles have their voluntary contractility, while their atrophy is usually due to the long inactivity to which they are subjected. Of course, certain movements are rendered difficult on account of the mechanical obstacle formed by the dislocated head of the humerus; but when reduction has been performed, the functional impediment seems to disappear.

In infantile paralysis muscular contraction to electric stimulation is notably diminished, if not completely absent, and the reaction of degeneration is always present. This research is most important and should remove all doubts as to the diagnosis, because in a true congenital dislocation all the muscles contract normally to the faradic and galvanic currents, and the reaction of degeneration is always absent. The prognosis of a congenital dislocation is not so serious as the monoplegic type of infantile paralysis, and if a careful study of the structures composing the joint is made, as well as of the muscles of the shoulder, in a large majority of cases that which belongs to a congenital condition and that which belongs to infantile paralysis can usually be made out. In all cases the muscular reaction and the presence or absence of the reaction of degeneration will allow one to make a correct diagnosis. I would say, however, that occasionally the fever usually observed in infantile paralysis may be absent. It also happens that the paralysis forms the first symptom. It may come on slowly and gradually increase, and then may slowly disappear without leaving any trace. Then the symptoms may reappear during the period of regres-

sion and the paralysis will extend to the bulb, resulting in death of the subject.

The condition of the ligaments of the shoulder-joint should be carefully examined, and it will be found that the changes that they have undergone almost always combine with the changes which have taken place in the bones. If the capsule is relaxed, the limb is very loosely hung, and the extent of its movements is considerably increased. If muscular action does not prevent, the head of the humerus may be displaced in all directions. If, on the contrary, the ligaments are shortened, they will prevent the movements of the joint, which will then be only partial.

The condition of the bones is not always an easy thing to ascertain, and in order to come to some conclusion the limb should be moved in all directions in order to explore the entire joint. The X-ray might be thought to be of value, inasmuch as it allows one to directly examine the condition of the joint; but if I had not made my clinical diagnosis of congenital dislocation of the shoulder before the radiograph was taken of my case, I believe that I should have been quite at a loss to know the exact condition of affairs had I been solely guided by the photographic picture of the skeleton.

The early methods of treatment which were applied to these cases practically consisted in a forced traction during a longer or shorter period of time, and immobilization of the joint after the dislocation had been reduced. From these considerations and also from what we know of the treatment of congenital dislocation of the hip, the following treatment may be employed if we are dealing with a very young child or a baby: hydrotherapy, cold affusions, massage, and electricity, which will keep the muscles well nourished, will certainly render considerable service; but with this a relative repose, and not an absolute one, should be given to the limb in order to prevent overfatigue and any action which might tend to draw the head of the humerus out of the cavity.

It would appear, however, that in the vast majority of cases the only satisfactory treatment will be surgical interference, and I propose here to briefly describe the operative technique for the reduction and permanent maintenance of congenital dislocation of the shoulder. The first operation that will be referred to is that advocated by the late Dr. A. M. Phelps, of New York, and is the one which was employed in the case here appended; but I would add that in my hands it was entirely unsatisfactory, inasmuch as the posterior incision made does not render the parts so accessible as if the joint were cut down on anteriorly, and for this reason other methods will be briefly described which will, I think, render the successful result of the operation an easier matter to attain.

Phelps' technique consists in an incision carried along the posterior border of the deltoid muscle, curving it downward. This gives a flap which its originator claimed readily exposed the head of the bone; but this is really far from the fact, as the joint is reached with difficulty. The capsule is then incised, and the head of the bone will be found under the spine of the scapula. It is stated by Marsten and Phelps that it is necessary to cut away about two-thirds of the head of the bone, or, in other words, down to the epiphyseal line. The bone should be rounded off like the original head, and then slipped into the glenoid cavity. The entire new articulation which has been formed by the head of the bone is next excised with a chisel or curette. The redundant capsule is then cut away and the capsule closed with catgut sutures. The limb should be put up in plaster, with the elbow well back and the arm at a right angle with the body.

A criticism that I would make is that from most recorded cases where operation has been undertaken, excision of the head of the humerus seems an unnecessary addition, for in these cases, including my own, the joint cavity and head of the bone were not sufficiently changed to necessitate any operative measures directed to the reduction.

That the capsule will always be found stretched or elongated is probably quite true in the majority of cases, and it is quite proper to reset enough of the capsule so that when it is stitched together it will cover the head of the humerus in a physiological manner.

There has been a large number of methods described and employed for gaining access to the shoulder-joint; three especially have been used. Langenbeck advocated the axillary region because it was more direct, since the head of the humerus is quite superficially located in the axilla and, consequently, easily attained. But this advantage is insignificant if one takes into consideration the many inconveniences that this incision presents, when it is essential to recognize and overcome the cause preventing reduction. There is also some danger of wounding the nerves and the vessels in this region, and on account of many other operative difficulties that have been reported by able surgeons this method has been more or less abandoned.

The posterior route has been particularly advocated by Nélaton and also, as we have seen, by Phelps. This is certainly an improvement over the axillary method. Nélaton's technique consists in making a horizontal incision on the external border of the acromion, and to this incision another one is joined at the posterior tip, directed downward toward the arm and following the direction of the muscular fibres of the deltoid (Fig. 1). By this combined incision a large cutaneous muscular flap is formed, which when thrown back gives a ready access to the posterior aspect of the region of the shoulder. It would, however,

appear that this posterior incision is in no way preferable to an anterior incision, especially if a forward dislocation exists.

On the contrary, with the anterior incisions this difficulty no longer exists, because the joint is attacked directly at the most desirable point. The technique that seems to me the most recommendable is that indi-

FIG. 1.



Nélaton's incision.

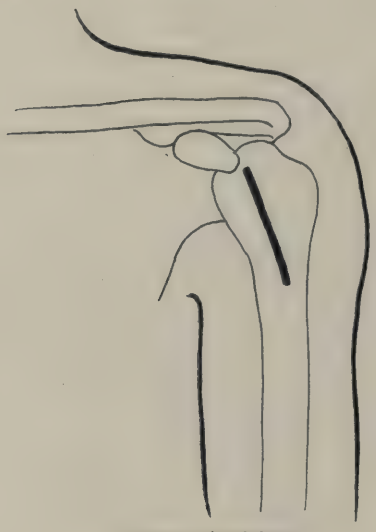
FIG. 2.



Duplay's incision.

cated by Duplay, and is as follows: A horizontal incision is made over the external border of the acromion and is begun just within the acromio-clavicular joint, and carried backward to the origin of the spine of the scapula. A second incision starts from the anterior tip of

FIG. 3.



Ollier's incision.

FIG. 4.



Perrin's incision.

the first one and is carried downward and outward, following the direction of the fibres of the deltoid muscle, to which it runs parallel. The upper lip of the horizontal incision is dissected off as far as the acromion, and the external end of the clavicle is exposed. The acromion

is then sawn through at the point of continuity with the spine of the scapula, and the clavicle is then cut through in the neighborhood of its articulation with the acromion. The deltoid thus becomes mobilized with its upper insertion, and may, consequently, be pushed aside so that the shoulder-joint is freely exposed. Such a free operation may not always be necessary, in which case Ollier's anterior incision may be employed, as seen in Fig. 3; but as this is well known, a description of the technique seems unnecessary.

The incision proposed by Perrin, Demons, Senn, and others is horizontal and transverse. It is commenced at the border of the acromion, passes 5 millimetres below the point of this apophysis, and is carried directly to the point of the coracoid. The deltoid is incised in the same direction and pushed downward by a retractor. By this means the fibrous tissues opposing the reduction of the head of the humerus are exposed. Although this method has been employed with success by some operators, I cannot believe that it will ever become popular.

P. H., aged five years, was brought to me for a lesion of the right arm, which was noticed for the first time several days after his birth.

Regarding alcoholism, syphilis, or tuberculosis in the family, all was negative, and there were three other children, one older and two younger than the patient, who were in every way perfectly developed. The mother only did her housework and had received no injury during pregnancy. The father was a healthy man, and had never had any serious sickness. Nothing was noted in the history of other members of the family.

The child was born normally at term, without forceps. He was well built; but a day or two after the birth it appeared to the mother that there was something wrong with the right arm, as the child appeared to lack the use of it. When the hand was seized and the arm raised, it would fall immediately upon being released. When moved it did not seem to cause pain, as the child did not cry, and it was noticed that when left alone the arm was not endowed with any spontaneous movement. The physician of the family consulted at this time did not appear to have examined the arm, and simply recommended the use of a sling. As the child grew the movements of the limb began to appear, but were limited; those of the hand and of the wrist and elbow only appeared to be normal. An impotency of the shoulder-joint has been present, so that the child could not reach his mouth with his hand, and was obliged to bend the head forward in order to touch his lips.

Examination of the patient showed a well-formed boy. He walked perfectly well, and the left arm was functionally normal and anatomically was perfect.

Examination of the diseased limb showed a marked difference between the left side and the right. The anterior aspect of the right shoulder had lost its rounded form and appeared less broad, while the distance separating the internal extremity of the clavicle and the projection of the stump of the shoulder was shorter than on the normal side. The height of the axilla was also diminished, and the subclavicular hollow

was more accentuated on this side than on the left. The points of both scapulæ projected distinctly backward, and on the right the point of the bone projected very distinctly. On the right the internal border of the scapula approached the spinous apophyses, and from the fact of its ascension the right scapula appeared as if atrophied; but this was simply an illusion, because by measurement it was found to be identical on both sides in both its vertical and horizontal diameters. Movements given to the right arm were transmitted to a great extent to the scapula. Inspection of the posterior aspect of the shoulder showed an abnormal projection just below the base of the acromion.

FIG. 5.



When left alone the arm hangs by the side of the body in slight abduction, the elbow being about 6 cm. from the thorax. The limb is in very marked internal rotation. The anterior aspect of the elbow has become internal, and faces the thoracic wall, while the epicondyle is directed forward and the epitrochlea backward, and the olecranon.

By palpation the external end of the clavicle and acromion are easily made out, under which a very depressible hollow is found which increases when the limb is abducted. Somewhat forward and below the acromio-clavicular vault a bony projection can be distinctly felt, recalling the shape of the coracoid apophysis. Over the posterior projection one feels that the teguments are pushed up by a bony projection of a

rounded form, and which participates in the movements given to the lower end of the humerus. This projection, on account of its shape, size, and mobility, impresses one as being the head of the humerus.

As to motion, abduction can be accomplished to quite an extent, but during this movement the arm is carried forward and cannot be projected backward. With the greatest effort the boy cannot raise his hand to his mouth or neck. Sensation is intact throughout the entire right arm, and trophic disturbances are wanting. Both radial arteries give a beat equal in strength and synchronous, so that any suspicion of vascular compression of the diseased side is eliminated. Electrical examination of the muscles shows that the periarticular muscles have preserved their reaction to both the faradic and galvanic current. Reaction of degeneration is absent, and the muscles are not contracted, showing that infantile paralysis is out of the question.

My diagnosis was congenital dislocation of the shoulder-joint, and in order to complete the diagnosis a radiographic picture of the thorax and both shoulder-joints was taken.

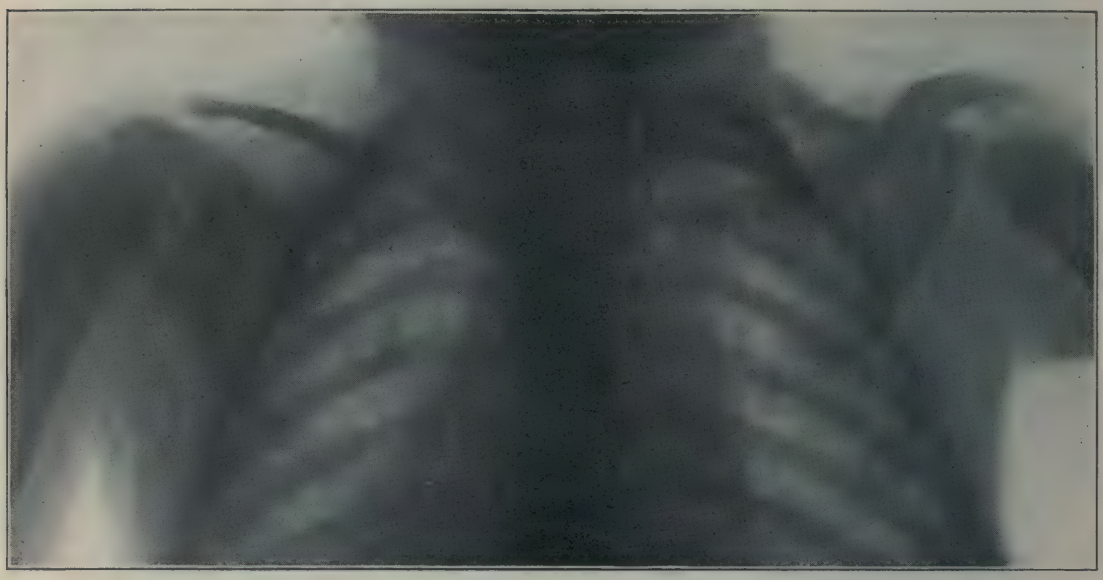
FIG. 6.



Operation was advised, and was done in April, 1901. The joint was exposed by Phelps' incision and the capsule opened. The head of the humerus presented only a very slight degree of atrophy, and the same was true of the glenoid cavity. After breaking up some adhesions the dislocation was readily reduced and the redundant capsule freely resected, after which it was closed with catgut sutures. A plaster dressing was applied, with the elbow held back, which was removed at the end of three weeks.

At the present time the result is most satisfactory. Examination of the child in June, 1902, showed that considerable use of the arm had been gained. He can now feed himself with the right hand and touch his forehead; the hand, however, cannot be placed on the top of the

FIG. 7.



head. Backward movements are improved, although not as perfect as might be desired; but, on the whole, the ultimate result of the operation has been more than satisfactory.

A CASE OF MYELOGENOUS LEUKÆMIA, WITH SEVERAL UNUSUAL FEATURES (ABSENCE OF EOSINOPHILIC LEUCOCYTES).

BY CHARLES E. SIMON, M.D.,
OF BALTIMORE, MD.

THE following case of leukæmia, which I have been able to follow for a period of nearly eighteen months and which recently came to a termination, presents a number of interesting features that warrant its publication in some detail.

C. T. F., aged forty-two years; married; printer.

Family History. Mother living; father died of meningitis (cerebral?).

Personal History. The patient has always been in good health and strong, excepting an attack of dysentery which occurred about twelve years ago. This has been followed by several attacks, the last one about eighteen months ago. After the diarrhœa ceased his strength was very slow in returning; he was readily fatigued by any effort, both physical and mental. When I first saw the patient (October 24, 1900) he complained of the passage of mucus in the stools, some pain after eating, general lassitude, and some degree of nervousness. The

appetite was not very good, and the bowels inclined to constipation. There was no nausea or vomiting. The pain occurred not only after meals, but at times also without regard to the taking of food. There was no pain during defecation and no blood in the stools. He had lost about ten to fifteen pounds; his usual weight is 140 to 145 pounds.

Examination at this time revealed the following condition: The patient is a well-built man, about five feet six inches in height, weighing 131 pounds. His color is sallow, but at this time I was not struck by the existence of a special grade of anæmia. The tongue was somewhat pale and moderately furred. Examination of the thorax showed no abnormalities. The abdomen was soft, nowhere painful, and the liver and spleen not palpable. Examination of the urine at this time was negative, and examination of a stool a few days later showed nothing unusual. At that time there was no mucus visible with the naked eye, and no blood. It was partly formed and of a natural color.

The patient was placed on a diet from which butchers' meat and carbohydrates in excess had been excluded, and ordered nux vomica; he was also instructed to use oil injections. On November 24th he reported that his bowels had been normal and regular since he began with the oil injections, three weeks ago. He feels much better in general, and has gotten over his feelings of weakness and inertia practically altogether.

The patient was then not seen until January 4, 1901, when he returned, as he said, to report that he was feeling quite well and had had no further trouble with his bowels. It was then noticed that his color was decidedly below par, and a hæmoglobin estimation showed but 40 per cent. (Fleischl), while the red corpuscles were down to 1,350,000. His leucocytes did not appear to be much increased at that time. A differential count showed about 6 per cent. of neutrophilic myelocytes and no eosinophilic cells or mast cells whatever, so far as I can remember. There was a fair number of normoblasts, and, after prolonged search, a few megaloblasts were also seen; some red cells were undergoing granular degeneration, and a number of polychromatophilic red cells were likewise encountered. There was some poikilocytosis, though not of high grade, and no decided tendency either to oval form or over size.

The patient at that time weighed 131 pounds. His color was not yellowish, but very pale, especially his ears, which appeared almost bloodless. Careful inquiry at this time into any possible causes of his anæmia failed to elicit any information of importance. He had been exposed to lead some years ago, but had never had any symptoms and had not worked in lead for a number of years. Another careful examination of a stool after a purge showed nothing of moment. He denied ever having had syphilis. He has had no hemorrhages, and there were no piles. He also stated that he had never had much color, but that possibly he was paler than usual since the foregoing summer. He stated at this time that his sexual desire was much impaired during the past six months. He was placed on Blaud's pills in increasing doses and the nux vomica continued.

January 22*d* his hæmoglobin had diminished to 35 per cent., while the myelocytes had increased to 9 per cent. Fowler's solution was then started.

29*th*. No change.

Although the patient was urged to report at regular intervals, he

was not seen again until March 9th. He then stated that he had really been feeling quite well and had noticed no special effect from the arsenic, and had discontinued it, after having taken from three to five drops for a couple of weeks. The hæmoglobin was now 27 per cent., and the myelocytes 12 per cent. The weight was 130 pounds. Examination of the abdomen showed no splenic enlargement. There was no glandular enlargement anywhere, and no tenderness on percussion over the bones. The urine was negative.

After this the patient was not seen until June 3d, when Dr. W. S. Thayer saw him in my absence. At that time the following note was made: Patient is well nourished; color very pale; not yellowish; lips and mucous membranes strikingly pale; tongue reddish in the middle, pale on edges. Thorax symmetrical, costal angle about 90°; resonance clear in front and axillæ; respiration clear. Heart: Point of maximum impulse in the fifth, just inside the nipple line; no enlargement of dulness to the right; first sound accompanied by a blowing, systolic murmur, lost in the mid-axilla; second sound clear. Murmur is feebler at the tricuspid; well marked at the aortic and pulmonic orifices. Abdomen natural; liver just palpable below the costal margin—about a finger's breadth below the costal margin on deep inspiration. Patient has rather a sallow, grayish anæmia.

A fresh specimen showed considerable differences in the size of the corpuscles; a good deal of poikilocytosis, but not as much as one commonly sees in pernicious anæmia; well-marked leucocytosis. The blood record of the dried specimens was unfortunately lost. Color index was not increased. There were slightly over 2,000,000 red cells. There was a distinct polynuclear leucocytosis (?). The patient was ordered Blaud's pills, plenty of milk, and a vacation in the Adirondacks. He returned in August, looking decidedly better, and was ordered to continue Blaud's pills. On October 15th Dr. Thayer saw him once more and noted that the patient was feeling much better and had gone back to his regular business. Red corpuscles then 3,968,000, leucocytes 14,000, and hæmoglobin 40 per cent.

After this I saw the patient again on January 11th, when he returned to see "just where he stood." He looked very pale, but did not complain especially beyond feeling a little fagged and readily becoming short of breath on exertion. The systolic murmur at the apex was then quite distinct, and was heard all over the precordia. The spleen could be felt a little below the costal margin; the liver was not palpable.

Red cells, 1,636,000; leucocytes, 10,200; ratio of whites to reds, 1:162. Hæmoglobin, 35 per cent. A differential count of 591 leucocytes gave the following result (eosinate of methylene blue):

Small mononuclears	11.9	per cent.
Large mononuclears and transition forms	7.9	"
Polymorphonuclear neutrophiles	50.7	"
Eosinophiles	0.0	"
Neutrophilic myelocytes	29.1	"
Mast cells	0.1	"

While counting the leucocytes seven normoblasts were seen and three megaloblasts; it was observed that in many of the normoblasts the nucleus was merely surrounded by a little hood-like appendage of polychromatophilic protoplasm. The nuclei were decidedly pyknotic.

There was a fair grade of granular degeneration, but not so extensive as we commonly see it in cases of well-advanced pernicious anæmia.

The patient was urged to attend to his condition more carefully, to resume his arsenic, and to rest.

On January 15th he saw Dr. Thayer, who then confirmed the condition of the spleen. He notes: the abdomen is natural; the spleen not visible. On deep inspiration, when the ribs are pressed behind, the spleen extends about four centimetres below the costal margin, but it sinks back during inspiration about to a level with this. There is no enlargement of the cervical glands. The point of maximum cardiac impulse is in the fifth space inside the mammillary line, about eight centimetres from the median line. The first sound is a little flapping, with a very soft systolic murmur which is lost as one reaches the anterior axilla, where the sound is decidedly flapping in character. At the base the systolic murmur is barely heard. There is an intense venous hum in the neck over the jugulars, more marked on the right than on the left, and disappearing in the recumbent posture. Recumbent posture brings out the soft systolic murmur at the aortic area and also in the pulmonary, and intensifies that at the apex. Liver not enlarged; flatness not below the costal margin in the mammillary line.

Dried specimens stained with the triple stain show rather marked poikilocytosis; the average size of the corpuscles is apparently normal; a considerable number of nucleated red corpuscles, mostly normoblasts; two very large megaloblasts were seen; one of them showed a nucleus clearly in the process of karyokinesis (aster); another showed two large deeply staining nuclei side by side, evidently having just divided. There were a certain number of nucleated red corpuscles with fragmented nuclei. There was very marked leucocytosis. A differential count of 1000 leucocytes showed:

Small mononuclears	14.3 per cent.
Large mononuclears and transition forms	7.2 "
Polymorphonuclear neutrophiles	47.8 "
Neutrophilic myelocytes	30.3 "
Mast cells	0.2 "
Eosinophiles	0.0 "

Many of the myelocytes were small elements scarcely larger than an ordinary polymorphonuclear leucocyte, although some large typical forms were seen. No eosinophiles were seen in fully an hour and a half's study of two specimens.

January 25th. Condition unchanged. Red cells, 2,080,000; leucocytes, 8950; hæmoglobin, 30 per cent. A differential count of 1000 leucocytes gave the following result (eosinate):

Small mononuclears	10.8 per cent.
Large mononuclears and transition forms	4.9 "
Polymorphonuclear neutrophiles	44.9 "
Neutrophilic myelocytes	39.4 "
Mast cells	0.1 "
Eosinophiles	0.0 "

While counting the 1000 leucocytes, fifteen nucleated red cells were seen, of which three were megaloblasts.

February 8th. The hæmoglobin has fallen to 20 per cent. (Fleischl). Red cells, 1,600,000.

Small mononuclears	7.9 per cent.
Large mononuclears and transition forms	7.0 "
Polymorphonuclear neutrophiles	46.7 "
Neutrophilic myelocytes	37.4 "
Mast cells	0.8 "
Eosinophiles	0.0 "

Granule cells were quite numerous, and polychromatophilia pronounced. Nucleated red cells were mostly of the normoblastic type, but a few megaloblasts were also seen. Most of the nucleated cells were markedly polychromatophilic, and the protoplasm surrounding the nucleus often disintegrating; in many merely showing like a shaggy hood.

The patient does not feel so well, and appears more inclined to give up his work and to rest on his back. He continues on arsenic, but has not gotten beyond five drops. The condition of the spleen remains unchanged. There is no enlargement of the inguinal glands; the liver is not palpable; there is no tenderness over the bones; no hemorrhages of any kind.

24th. The patient has had an attack of diarrhœa lasting several days. The arsenic is reduced from seven to three drops. Hæmoglobin is 28 per cent. (Dare); the leucocytes number 22,600, the highest number yet reached. A differential count of 896 gave the following result (eosinate):

Small mononuclears	9.0 per cent.
Large mononuclears and transition forms	7.1 "
Polymorphonuclear neutrophiles	30.1 "
Neutrophilic myelocytes	53.5 "
Mast cells	0.0 "
Eosinophiles	0.0 "

Megaloblasts were again seen in small numbers. Granular and polychromatophilic degeneration pronounced. The patient has been resting since last note, and realizes that his condition is serious.

An examination of a stool on March 11th disclosed nothing of interest; there were no ova of parasites. Examination of a specimen of urine for the first time shows a very small amount of albumin (serum albumin and serum globulin); there is no Bence Jones albumin. On microscopic examination an occasional hyaline cast is seen. There is no polyuria. Specific gravity, 1016. Sugar absent. Indican not increased.

March 18th. The patient has been on his back and in the open air, on his veranda, most of the time. Hæmoglobin, 34 per cent. (Dare); red cells, 2,842,000 (!); leucocytes, 25,650. A differential count of 581 leucocytes gave the following results (eosinate):

Small mononuclears	5.1 per cent.
Large mononuclears and transition forms	8.2 "
Polymorphonuclear neutrophiles	42.5 "
Neutrophilic myelocytes	43.5 "
Mast cells	0.5 "
Eosinophiles	0.0 "

Granular degeneration was well marked, some of the cells presenting unusually large granules and little, irregular rods. Normoblasts were

common; megaloblasts as in previous examinations. All the nucleated red cells practically were polychromatic, and most of them provided only with a shaggy, narrow zone of degenerating protoplasm.

The patient was told to continue his rest and to be out-of-doors as long as possible and whenever possible. He continues his arsenic.

April 14*th.* He has stopped his arsenic for a few days, as his appetite became impaired, and he had another attack of diarrhœa. He has now been on his back for nearly eight weeks. Condition otherwise unchanged. Hæmoglobin, 42 per cent.; red cells, 2,100,000; leucocytes, 10,500. A differential count gave the following results (eosinate):

Small mononuclears	10.8 per cent.
Large mononuclears and transition forms	8.3 "
Polymorphonuclear neutrophiles	44.4 "
Neutrophilic myelocytes	36.0 "
Mast cells	0.5 "
Eosinophiles	0.0 "

May 14*th.* In order to obtain a more bracing air and to be out-of-doors more, the patient went to Atlantic City. He returns looking much better, sunburned. He feels much better. His spleen is readily to be felt below the costal margin. No glandular enlargement. Liver not palpable. Urine shows a very small amount of albumin; there is no Bence Jones albumin. No pain in the bones, either spontaneous or on percussion. Condition of heart as before. A differential count of 653 leucocytes gave the following results (eosinate):

Small lymphocytes	8.2 per cent.
Large lymphocytes	9.0 "
Large mononuclears (lymphoid cells)	13.5 "
Polymorphonuclear neutrophiles	41.6 "
Neutrophilic myelocytes	27.2 "
Mast cells	1.3 "
Eosinophiles	0,0 "

While counting the 653 white cells only five nucleated red corpuscles were met with; of these two were megaloblasts. The degree of granular degeneration was not so extensive as before, but polychromatophilic degeneration about the same. Some of the lymphoid cells (see below) were exceedingly large; one cell measured 15 x 17.5μ.

The patient then returned to Atlantic City. He was next seen, during my absence, by Dr. Thayer, to whom I am indebted for the following notes also:

June 15*th.* Patient was seen at his house with Dr. Smart. About a week ago he returned home from a trip to Atlantic City, feeling much improved. But about three days ago he began to have headache, fever, and in the mornings noticed a little blood in the mouth. Yesterday the gums became sore and the glands under the jaw began to enlarge.

The patient is in bed, sunburned; vessels on forehead seem unusually full; has a slight puffy look to his eyelids and a slight yellowish tinge to the complexion. The mucous membranes of the tongue are extremely pale. The gums in several places are swollen and black from hemorrhages into the tissue. The pulse is rapid and small; skin hot. The chest is clear in front and in the axillæ. Heart: Loud systolic murmur heard all over the cardiac area. Abdomen natural. The spleen reaches nearly to the umbilicus, nine centimetres below the

costal margin on quiet breathing. The liver is two fingers' breadth below the costal margin in the mammillary line. No tenderness over the long bones. The glands under the jaw are moderately enlarged and slightly tender. Small discrete glands are felt in all parts of the neck and axillæ. Inguinal glands slightly enlarged.

Hæmoglobin, 39 per cent.; red cells, 1,932,000; leucocytes, 116,000 (!). A differential count of 1000 leucocytes showed the following (triple stain):

Small mononuclears	4.18 per cent.
Large mononuclears and transition forms	29.8 "
Polymorphonuclear neutrophiles	17.9 "
Neutrophilic myelocytes	46.9 "
Mast cells	0.6 "
Eosinophiles	0.0 "

There is considerable poikilocytosis; a moderate number of nucleated red corpuscles, much fewer than in the January specimens; most of these were normoblasts, some with fragmenting nuclei. One large nucleated red corpuscle was seen, fully as large as a polymorphonuclear leucocyte, with a large deeply-staining nucleus. Over one-fourth of the leucocytes consist of large mononuclears and transition forms. These are large cells with rather pale nuclei, though in many instances the nucleus takes on a fairly deep color. The protoplasm is sometimes clear and colorless, but is more commonly stained a slightly lilac color. The nuclei are large, round, or bean-shaped, often with sharp, deep, nicks, sometimes dividing the nucleus into several irregular pieces. A considerable number of these cells showed true polymorphous nuclei with homogeneous lilac-staining protoplasm. These nuclei, however, were larger and paler than those of the polymorphonuclear neutrophiles. But one eosinophilic cell was seen on a careful study of two good specimens, and this was found only while studying the specimens with the low power to find nucleated red corpuscles. The myelocytes were, for the most part, very large and characteristic.

The Fowler solution, which the patient has been taking more or less constantly, was omitted, and arsenious acid (one-sixth grain) ordered in pill form, with iron. Mouth-wash of carbolic acid.

13*th*. Seen again with Dr. Smart. The patient has had continuously high fever from 101° to 104° F.; pulse to-day 110 to 130. The enlargement of the glands under the left jaw has increased. The skin is very yellow, and there is a fine petechial eruption on the forehead and face; less over the rest of the trunk and extremities. The patient is very weak, pulse at time of visit 128, small and of low tension. The gums of the lower jaw, about under the right canine tooth, show a wedge-shaped area about one centimetre in extent, which is black and necrotic; a smaller area about a carious bicuspid tooth in the upper jaw is also sloughing. There is a general stomatitis; the mucous membranes are covered in numerous areas by superficial white membranes. The mind is quite clear.

18*th*. The temperature has gradually fallen to normal, and the pulse has diminished in rate, being now from 100 to 110; but the patient has been very weak and has had difficulty in taking his food, partly on account of nausea, partly on account of the soreness of the mouth. The complexion is of a deep, sallow, yellowish color. More purpuric spots have appeared on the face and all over the body. The

spleen reaches to the umbilicus. The glands under the jaw are somewhat less swollen. The areas in the gums, which were previously black, are now suppurating freely, and there is an extensive foul suppurative, in some instances apparently gangrenous, stomatitis in different spots on the gums of each jaw. The patient lies in a dull apathetic condition, and when I came into the room asked me in a whisper to look out for the condition of his nerves, as if he feared that he was becoming delirious. The hæmoglobin was 32 per cent. Absolute counts were not made, but a superficial examination of the blood would suggest that the number of leucocytes had increased.

A differential count of 923 leucocytes which I made from specimens which Dr. Thayer kindly placed at my disposal gave the following results:

Small lymphocytes	0.6 per cent.
Large lymphocytes	0.5 "
Lymphoid cells	54.8 "
Polymorphonuclear neutrophiles	18.5 "
Neutrophilic myelocytes	25.0 "
Mast cells	0.4 "
Eosinophiles	0.0 "

While counting the 923 leucocytes no nucleated red cells were seen, but in otherwise studying the preparation a few were encountered. Granular degeneration was not noticeable at all, and polychromasia but little pronounced. Most remarkable was the large percentage of the "lymphoid" cells.

After Dr. Thayer's last visit the temperature rose again, but did not exceed 101.5° F. The pulse and respiration were about in proportion to the height of the temperature. The patient rapidly lost ground. There was much nausea and occasional vomiting, and on two occasions he complained of pain in the left side. There was some slight bleeding from the gums. Stupor became more and more marked; the pulse feebler and feebler, and death finally occurred in coma on June 22d. An autopsy was unfortunately not obtained.

CONDENSED TABLE OF BLOOD EXAMINATIONS.

Date.	Hb.	Color index	Total No. of red cells.	Total No. of leucocytes.	Lymphocytes.	Large mononuclear elements.	Polymorphonuclear neutrophiles.	Neutrophilic myelocytes.	Eosinophiles.	Mast cells.
1901					Per ct.	Per ct.	Per ct.	Per ct.	Per ct.	Per ct.
Jan. 4	40	1.5	1,350,000	not increased	.....	.....	.....	6.0	0	0
" 22	35	...	....	.....	.....	.....	.....	9.0	0	0
" 29	27	...	.....	.....	.....	.....	.....	12.0	0	0
June 3	...	...	2,000,000	increased						
Oct. 15	40	0.5	3,968,000	14,000						
1902										
Jan. 11	35	1.0	1,636,000	10,200	11.9	7.9	50.7	29.1	0	0.1
" 15	...	...	.....	.....	14.3	7.2	47.8	30.3	0	0.2
" 25	30	0.7	2,080,000	8,950	10.8	4.9	44.9	39.4	0	0.1
Feb. 8	20	0.6	1,600,000	.....	7.9	7.0	46.7	37.4	0	0.8
" 24	28	...	.....	22,600	9.0	7.1	30.1	53.5	0	0.0
March 18	34	0.6	2,842,000	25,650	5.1	8.2	42.5	43.5	0	0.5
April 14	42	1.0	2,100,000	10,500	10.8	8.3	44.4	36.0	0	0.5
May 14	...	...	.....	....	8.2	22.5	41.6	27.2	0	1.3
June 15	39	1.0	1,932,000	116.000	4.8	29.8	17.9	46.9	0	0.6
" 18	32	...	.....	very much increased	0.6	55.3	18.5	25.0	0	0.4

To recapitulate in brief we have a patient who becomes markedly anæmic while under general observation, without apparent cause, and who, barring a brief interval during which he seems to have gained some ground, steadily declines in health, and dies at the expiration of seventeen months from the time at which the anæmia was first noted. Subjectively, the patient presents no symptoms until well along in the course of the disease, and then he merely complains of shortness of breath on exertion and a gradually increasing though not very pronounced general weakness. Objectively, we find a very moderate enlargement of the spleen, which, however, only appears after several months, which then slowly increases, but becomes quite extensive toward the end. There is very little glandular enlargement, if any, until quite late in the course of the disease. The oligochromæmia is quite intense from the beginning and out of proportion to the diminution of the red cells. At first there is no hyperleucocytosis; later a moderate increase beyond the physiological maximum occurs, but toward the end this increase reaches very extensive proportions, the ratio of whites to reds falling to 1:16.6. Neutrophilic myelocytes are present from the beginning in notable numbers; they steadily increase until shortly before the end, when they diminish again, but even then do not fall below 25 per cent. There is a corresponding diminution in the number of the polymorphonuclear neutrophiles, and at the same time of the small mononuclear elements. Large mononuclear elements which, through the greater course of the disease were not present in notable numbers, became more numerous, and finally constitute 54.8 per cent. of all leucocytes. Mast cells were at first absent; later they appear, and with some fluctuations they steadily increase until the end. Of eosinophiles only two cells were found in the course of all the examinations, one of which was an eosinophilic myelocyte. Nucleated red cells, both of the normoblastic and megaloblastic variety, were present throughout the course of the disease, but notably much more numerous in the earlier stages. Toward the end but few were seen.

Early in the disease, when the anæmia was first discovered, I regarded the case as one of pernicious anæmia, but the steady increase of the myelocytes, the diminished color index, and the very manifest development of a hyperleucocytosis caused me to abandon this idea, and rather suggested a myelogenous leukæmia as the most likely diagnosis. The case is certainly unusual, however, and does not readily fit the frame of the picture of the disease as modelled by Ehrlich and Lazarus.[1]

The clinical history, to be sure, is not out of the ordinary, and even the slight enlargement of the spleen during the greater period of the

[1] Ehrlich-Lazarus. Leukaemie, etc., Nothnagel's Path. u. Therap, vol. viii., Part I., Heft 3.

disease is not incompatible with the diagnosis. Lazarus states that splenic tumor, though it is usually a dominating symptom, is not of constant occurrence in myelogenous leukæmia, and he cites a case of Litten in which there was only a minimal enlargement. Toward the end, moreover, our patient also presented a well-marked splenic tumor. The remarkable feature of the present case, however, was the condition of the patient's blood, and there are several factors which are here of special interest. First of all, it is noteworthy that until late in the disease there was no grade of hyperleucocytosis that was at all comparable to what is usual in myelogenous leukæmia. In the beginning, indeed, the number of the leucocytes scarcely exceeded the physiological maximum. This factor on first consideration would tend to render the diagnosis of a myelogenous leukæmia doubtful, as a very material increase has usually been regarded as a *sine qua non* in diagnosis. But in view of the large percentage of myelocytes, the clinical history of the disease, and the subsequent development of an extensive polyleucocythæmia, more especially, I scarcely think that this factor alone is capable of influencing our diagnosis. I have looked over the literature in search of still other cases of myelogenous leukæmia in which no very extensive increase of the leucocytes has been observed, and have found two cases which, in this respect at least, can be placed alongside of my own. One is reported by Michaelis,[1] and another by von Noorden.[2] In the first case the total number of leucocytes is given as 16,000, and is said to have remained fairly constant up to the time of death, while the ratio of whites to reds, varied between 1 : 215 and 1 : 150. This case, to be sure, was also not a typical case of myelogenous leukæmia, but rather occupied a position midway between the orthodox lymphatic and myelogenous varieties; nevertheless it was a leukæmia with very manifest involvement of the myeloid tissue (7 per cent. of neutrophilic myelocytes), and the appearance of numerous bone-marrow giant cells in many of the organs. In von Noorden's case, which was a typical instance of myelogenous leukæmia, and is so recognized by Ehrlich, the ratio of whites to reds, did not exceed 1 : 200. Such cases, however, are manifestly rare, and in a survey of the text-book literature on the subject I have not found any additional cases mentioned in which the number of the leucocytes was so low as in the earlier stages of my case. But, after all, there seems to be a growing tendency to attach only secondary importance to the actual number of the leucocytes in the diagnosis of myelogenous leukæmia, as the characteristic feature of the disease is in reality the appearance in the blood of cellular elements which are foreign to it under normal

[1] L. Michaelis. Ueber einen d. Gruppe d. Leukaemie-artigen Erkrankungen zugehörigen Fall, Zeitschr. f. klin. Med., 1902, vol. xlv. p. 87.

[2] Ehrlich and Lazarus, p. 118.

conditions. These elements are the myelocytes, and most important the neutrophilic variety. Upon their presence in considerable numbers, even early in the disease, both Dr. Thayer and I largely based our diagnosis. The occurrence of myelocytes *per se*, of course, would not warrant the diagnosis of a leukæmia, as they may be found in other conditions as well. In the acute infections they may thus appear, but their presence is then probably always associated with a very notable increase of the polymorphonuclear elements, which, indeed, dominate the blood picture. In our case, moreover, there were still other factors denoting serious disease affecting the hæmopoietic organs, which do not constitute a feature of the acute infections. The relative percentage of the myelocytes also increased to such a height as is never observed excepting in myelogenous leukæmia, and their increase in fact was one of the principal factors which caused me to abandon the diagnosis of pernicious anæmia, to which I had at first inclined. Many of the myelocytes were of the smaller variety with trachychromatic nuclei, but there were also present until quite late in the disease notable numbers of the large type with amblychromatic nuclei. Toward the end these latter appeared to be less numerous, and at that time, in fact, the blood picture was controlled to a great extent by the presence of mononuclear elements which were devoid of specific granules and which I have classified in my last differential counts as lymphoid cells. To these I shall return later.

Aside from the comparatively low leucocyte counts during the greater period of the disease, the most remarkable feature of my patient's blood was the practical absence of eosinophiles. I cannot say positively that they were absent early in the disease, as my blood counts from that period were unfortunately lost. My impression, however, is that even at that time they must have been greatly diminished, if not absent; eosinophilic myelocytes at any rate were certainly not observed. But from January, 1902, on I have positive records. I have myself examined many slides of the patient's blood for the sole purpose of discovering eosinophilic cells, and numerous examinations were also made by the gentlemen who were working in my laboratory at the time of the patient's illness, but only one eosinophilic cell was ever found—an eosinophilic myelocyte. In the various examinations which Dr. Thayer made one eosinophile also was only seen. Since the patient's death I have again gone over my preparations with the view of establishing an actual percentage of eosinophiles, but I have had no more success than before, and for practical purposes we can regard the eosinophiles as absent. Granting the correctness of our diagnosis, and I see no reason for abandoning it in view of the marked myelæmia which actually existed, this case represents, so far as I can see, the only case of myelogenous leukæmia with practical absence of eosinophiles that

has been recorded. This is, indeed, most remarkable, in view of Ehrlich's emphatic and frequently repeated statement that the absolute number of the polynuclear eosinophiles is invariably increased in myelogenous leukæmia. This doctrine of Ehrlich has been repeatedly assailed, but hitherto under the mistaken assumption that Ehrlich had reference to the relative number of the eosinophilic cells, when as a matter of fact he has only spoken of an increase in their absolute number. In the present case, however, we may properly say that there were no eosinophiles present in the blood at all. It thus appears that unless our diagnosis of myelogenous leukæmia is abandoned, and, as I have said, I can see no urgent reason for doing so, we must extend our conception of the disease so as to comprise the case under consideration. It might be argued that the absence of the eosinophiles in our case could have been referable to the existence of some septic complication, but, barring the terminal gingivitis, there was no clinical evidence whatever of any septic process at any time which was borne out, moreover, by the non-existence of a polynuclear neutrophilic hyperleucocytosis.

To illustrate the diagnostic value of an absolute increase of the eosinophilic cells in myelogenous leukæmia Ehrlich cites a case of bone-marow carcinomatosis, reported by Epstein,[1] in which a leukæmoid condition of the blood was noted, and "in which the absence of eosinophilic cells excluded the existenceof true leukæmia." In this case a notable increase of the leucocytes was noted, the ratio of whites to reds varying between 1 : 25 to 1 : 40; numerous nucleated red cells, both of the normoblastic and megaloblastic type were seen, and in addition there were present a considerable number of neutrophilic myelocytes. Of eosinophiles only two cells were found in all the preparations that were made in the course of fifteen days. In my own case there could be no question of the non-existence of malignant disease in the sense of a carcinomatous involvement of the bone-marrow. The clinical history and the course of the disease are entirely opposed to such an assumption, and suffice to exclude their existence, even though an autopsy was not made.

A further consideration also, which might suggest itself as a possible explanation of the case—*i. e.*, the existence of multiple myeloma of the bone-marrow, can be ruled out. That multiple myeloma may terminate under the picture of a leukæmia is possible, as shown by the case of Askanazy.[2] The absence of Bence Jones albumin, however, and the

[1] J. Epstein. Blutbefunde b. metastatischer Carcinose d. Knochenmarks, Zeitsch. f. klin. Med., 1896, vol. xxx. p. 121.

[2] This case, it is true, is usually cited to illustrate that the Bence Jones albumin is not absolutely pathognomonic of myeloma; but I must confess that the extensive rarefaction of the bone substance is, nevertheless, strongly suggestive of the disease.—S. Askanazy, Deutsch. Arch. f. klin. Med., 1900, p. 34.

fact that the patient at no time complained of pain in the bones, either spontaneously or on percussion, conjointly tend to throw out such a possibility in our case.

It seems to me, after carefully weighing all the possible explanations which could be offered of a blood find as we see it in our case on the basis of something else than a myelogenous leukæmia, that we must still adhere to our diagnosis, or we must admit that a non-leukæmic condition may exist in which neutrophilic myelocytes can occur in the blood to the extent of 46.9 per cent., corresponding to an absolute number of 54,404 (!), and in which the total number of leucocytes may reach 116,000 pro cbmm., coincidently with the existence of a splenic tumor reaching nearly to the umbilicus. A concurrence of these three factors has, so far as I know, not been observed outside of myelogenous leukæmia, and we are thus forced to the conclusion that, after all, cases of the disease may occur in which the eosinophiles are neither relatively nor absolutely increased. I have looked over the literature so far as it was accessible to me in the attempt to find a parallel case to my own, but have not been successful. I have, however, met with at least one instance of leukæmia with undoubted involvement of the bone-marrow, in which a total increase of the eosinophiles likewise did not exist, and which in a measure may be regarded as illustrating an intermediary stage of the disease between the typical myelogenous variety with absolute eosinophilia, and my own case. This case is that of Michaelis,[1] already referred to. With a leucocytosis of 16,000, the percentage of eosinophiles was only 0.4, thus corresponding to a total of 64 cells, as compared with a maximum normal of 250, as given by Zappert.[2]

Equally striking at first as the absence of eosinophiles in my case was the low percentage of the mast cells, and, early in the disease also, their low absolute numbers. I dwell on this in view of Ehrlich's statement that the mast cells are absolutely increased in all cases of myelogenous leukæmia, and that their presence in increased numbers is even more important from the standpoint of differential diagnosis than that of the eosinophiles.

But, while their number at first was not only relatively but also absolutely low, a definite increase occurred later in the disease. Still, as late as January 11th the total number was only 10 per cbmm., and on January 25th even less—*i. e.*, 8.9 per cbmm. A relative increase then occurred to 0.8 per cent., which was followed by a decrease to zero on February 24th. By March 18th, however, they had increased to 0.5 per cent., corresponding to a total of 128, and on May 14th, 1.3 per cent. were counted. The last absolute count was made on June

[1] Michaelis. Loc cit.

[2] J. Zappert. Ueber d. Vorkomen d. eosinophilen Zellen im anaemischen Blut. Zeitsch. f. klin. Med., 1893, vol. xxiii.

15th, when the percentage was only 0.6, but the total number 696! We thus see that at a time when the disease was fully developed there existed a very marked increase of the mast cells, which fact still further strengthens our assumption that the case was in reality one of myelogenous leukæmia.

In conclusion, I wish to refer to the decided increase of the mononuclear elements devoid of granules which occurred toward the end of the disease, when fully 55 per cent. of all leucocytes belonged to this category. Of these, moreover, 54.8 per cent. were of a type which manifestly is distinctly different from the large mononuclear elements of normal blood. This difference, to be sure, is not so apparent in preparations that have been stained with Ehrlich's triple stain, but it becomes very manifest in specimens that have been stained with the eosinate of methylene blue which, after all, is much better adapted to the study of the mononuclear elements. The exact position which these cells occupy among the elements of the blood is still a matter of dispute. They are certainly not identical with the common, small lymphocytes, as they lack the narrow rim of deeply-staining basophilic protoplasm, the sharply defined nucleus, and as they are much larger in size. In 1895, Fränkel[1] described a type of cell as occurring in acute (lymphatic) leukæmia, which corresponds to our form more closely. These cells are large and provided with a large, feebly-staining, round or karyolobic nucleus which is surrounded by a narrow zone of non-granular basophilic protoplasm. He regarded these cells as large lymphocytes and as derivatives of the common smaller variety. Similar cells have been observed in the germinal centres of lymph glands, and were termed by Benda[2] lymphogonia, while corresponding cells which he found in the bone-marrow were designated as myelogonia. These latter in turn are possibly identical with Troje's[3] marrow cells, and Grawitz's[4] "immature" cells, of which he supposed that under certain conditions they might take up granules and thus become myelocytes. The normal occurrence of non-granular mononuclear leucocytes in the bone-marrow, which was still doubted, has now been definitely established through the researches of Pappenheim,[5] Rubinstein,[6] and others, and it is quite likely that all these various types are in reality identical and to be distinguished from the common lymphocytes and large mononuclear leucocytes of the blood. Nägeli,[7] also,

[1] A. Fränkel. Ueber akute Leukaemie, Deutsch. med. Woch., 1895, Nos. 39–45.
[2] Benda. Anat. Mittheil. über acute Leukaemie. Verhandl. d. 15 Cong. f. inn. Med., 1899.
[3] Troje. Ueber Leukaemie u. Pseudoleukaemie. Berl. klin. Woch., 1892, No. 12.
[4] Grawitz. Klinische Pathol. d. Blutes, 1896.
[5] Pappenheim. Ueber Lymphaemie ohne Lymphdrüsenschwellung. Zeitsch. f. klin. Med., 1900, vol. xxxix. p. 171.
[6] Rubinstein. Zeitsch. f. klin. Med., 1901, vol. xliii. p. 161.
[7] Nägeli. Ueber rothes Knochenmark u. Myeloblasten. Deutsch. med. Woch., 1900, No. 18.

does not regard the non-granular cells of the normal bone-marrow as a species of lymphocytes, but as specific bone-marrow cells, which he terms myeloblasts, and, like Pappenheim, regards as antecedents of Ehrlich's myelocytes. As he has pointed out, these cells are found in the blood in every case of myelogenous leukæmia, and may in the later stages, as in our case, represent the greater proportion of all the leucocytes. Michaelis and Wolff[1] term these cells lymphoid cells, in contradistinction to the lymphocytes of the blood; they wish to convey the idea that the bone-marrow lymphocyte is still capable of a relative differentiation, while this is no longer possible in the case of the common lymphocyte of the blood. Pappenheim regards these cells, which correspond to his large lymphocytes, as the mother cells of the small lymphocytes, of the red cells and of the myelocytes, and, as I have said, it seems well established that these cells are normally found not only in lymph glands and other organs of the body, but also in the bone-marrow. With these cells, I think, the "large mononuclear" elements in my case are identical. As I have said, they differ markedly from the common lymphocyte, and they certainly do not resemble the ordinary large mononuclear elements of the normal blood. It might, of course, be suggested that these large mononuclear elements, which, with Wolff and Michaelis, I shall term lymphoid cells, represent myelocytes that have lost their neutrophilic granulation. That such an occurrence may be possible is undoubted. Zappert,[2] Ehrlich-Blachstein,[3] and Arneth[4] have described such cases, and Ehrlich,[5] himself, reports on the absence of neutrophilic granules in the polynuclear leucocytes in a case of post-hemorrhagic anæmia. Everyone, moreover, who has busied himself to any degree with the study of the blood in pathological conditions will have observed that under certain conditions the amount of neutrophilic material is very much diminished. Sometimes, it is true, this is only apparent, and it may be possible by a suitable modification of technique to bring out the granules even in cases in which they appear to be absent. An explanation of such anomalous conditions cannot be given; but, as I have said, everyone who has busied himself to any degree with such matters is perfectly familiar with their occurrence. In my case, however, this explanation certainly does not hold good, even though a marked diminution of the neutrophilic material had also occurred toward the end of life. That they may be related to the myelocytes I do not wish to

[1] Michaelis und Wolff. Die Lymphocyten. Deutsch. med. Woch., 1901, p. 651.
[2] Cited by Ehrlich-Lazarus. Die Anaemie Loc. cit., p. 126.
[3] Ehrlich-Blachstein. Ibid., p. 126
[4] Arneth. Haematologische Befunde zu Leube: Ueber einen Fall von rapid verlaufender schwerer Anaemie mit gleichzeitiger leukaemischer Beschaffenheit d. Blutes. Deutsche Arch. f. klin. Med., vol. lxix., Heft 3 and 4.
[5] Ehrlich. Die Anaemie, p. 89.

deny, for we meet with cells, on the one hand, in which the protoplasm begins to show a decided granular appearance, the granules staining with basic dyes, and, on the other hand, we see cells of this second type in which neutrophilic granules are just beginning to appear and in which the protoplasm is scarcely basophilic at all, but is beginning to show distinct oxyphilic tendencies.

In much of the past work on the morphology of the blood in myelogenous leukæmia sufficient attention has not been directed to the mononuclear non-granular elements which appear in the circulating blood, and most observers have contented themselves with describing such elements as large mononuclear leucocytes. So long as the tendency exists to employ only the "allein-selig-machende" triple stain of Ehrlich, as Pappenheim quaintly terms it, but little progress is to be anticipated, from the clinical side, in the attempt to clear up the mooted question of the classification of the leukæmias. Some work, however, has been done to break through the rigid barriers which Ehrlich and his school have erected between the lymphatic and the myelogenous varieties, and, so far as the blood picture can serve as a basis of classification, there seems to be good ground for the recognition of three forms of leukæmia, as Reed[1] suggests, which are all due to myelogenous changes. These forms may be known as the myelogenous, the lymphoid and mixed-cell varieties, all of which in turn may be either acute or chronic, the general tendency of the first being toward chronicity and of the second toward an acute course. It appears, moreover, that cases of the first order may pass over into the second type, though the reverse has not been definitely proven. Cases representing the mixed-celled variety will probably become more frequent when clinicians will have learned to depend not only on the triple stain, but to carry their differentiation beyond its limits. Cases of this order have been reported by Michaelis[2] and Wolff,[3] and possibly the cases of Bloch and Hirschfeld,[4] and that of Arneth[5] also belong to this category.

To attempt an explanation of the absence of the eosinophiles in the present case seems scarcely practical, especially as no autopsy was had, and we are unable to affirm that the production of eosinophilic cells was actually arrested. That such was the case, however, seems a fairly logical inference, in view of the fact that eosinophilic myelocytes also

[1] D. M. Reed. Acute Lymphatic Leukæmia without Enlargement of the Lymph Glands, THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, 1902, vol. cxxiv. p. 653.

[2] Loc. cit.

[3] A. Wolff. Ueber d. Bedentung d. Lymphoidzelle b. d. normalen Blutbildung u. b. d. Leukæmie, Zeitsch. f. klin. Med., 1902, vol. xliv. p. 385.

[4] Bloch and Hirschfeld. Zur Kenntniss d. Veränderungen am Centralnerven-system b. d. Leukaemie, Zeitsch. f. klin. Med., 1900, vol. xxxix. p. 32.

[5] J. Arneth. Loc. cit.

did not appear. The absence of the polynuclear variety might be explained on the basis of negatively chemotactic influences being at work (contrary to the usual, to be sure), in which case their production need not have been arrested. But this explanation can hardly be applicable in the case of the eosinophilic myelocytes, if, with Ehrlich, we regard all mononuclear cells as not subject to the law of chemotaxis.

THE DERMATOSES OCCURRING IN EXOPHTHALMIC GOITRE.*

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The dermatoses occurring in the group of affections commonly described in this day as belonging to "inner medicine" do not always sustain definite relations to what may be termed the essential morbid process. Some cutaneous manifestations, as, for example, in the exanthematous fevers, are more or less constant syndromes of the systemic condition. Others, as the xanthoma of glycosuria, are the rare and exceptional concomitants of the general disease.

It is the last-named group of disorders the etiological relations of which are to be viewed with caution if not suspicion. Given such a malady as Asiatic cholera, in which by far the larger number of victims exhibit no changes in the skin, the inference is natural that in the exceptional cases the intervention of some novel and accidental agency has wrought the unusual result.

These considerations have force in relation to exophthalmic goitre, known also as Basedow's or Graves' disease, an affection for the most part unaccompanied by skin symptoms, and yet one which at times exhibits in the course of its evolution changes in the integument of the highest importance. For example, under the title "Cutaneous Affections Occurring in the Course of Graves' Disease," S. E. Dore[1] in 1900, published a valuable report of leucodermatous and other changes in the skin occurring in coexistence with exophthalmic goitre; the author also presenting a survey of the literature of the subject at the date of his paper.

As to the essential or accidental connection of these cutaneous syndromes with the general pathological state, a due reserve can be admitted by recognizing the fact that with respect to the other ailments of the

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general economy the tegumentary symptoms may be somewhat loosely classified as follows:

In a first group may be named the dermatoses which represent a purely accidental concurrence with symptoms indicative of the general ill health of the subject of the disease. Thus, for example, patches of tinea versicolor may be seen on the surface of the chest of a patient suffering from pulmonary tuberculosis.

In a second group may be included those changes in the skin which are more or less *distantly* related to the essential morbid process. The cutaneous symptoms may be directly due to a non-cutaneous manifestation, which in turn is dependent upon some factor more nearly related to the causal element in the general disease. Thus the sudamina of typhoid fever are the remote outcome of the fundamental morbid process—*i. e.*, infection with the bacillus of typhoid; for several intermediary conditions are traceable, each one of which is more or less essential to that which follows it. A concise expression of the evolution would be as follows: typhoid infection, impression on nerve centres, vasomotor instability, hyperidrosis, sudamina.

In a third group may be recognized those morbid symptoms in the skin which are *intimately* related to the systemic disease. In illustration of the disorders here classed may be cited the exanthemata and the purpuras of septic infection, in all of which the result is produced by the direct action of the specific organism or its toxines on the structures composing the skin.

To one or another of these categories may be assigned, together with the cases the brief records of which are appended, the histories in medical literature of similar import.

Case I. *Exophthalmic Goitre and Hidrocystoma.* Mrs. L. D., thirty-nine years of age, married eleven years and mother of two living and healthy children, had had three miscarriages. She weighed 156 pounds and had previously enjoyed good health. She consulted one of us first in 1884, for relief of a vulvar ulcer which was believed by herself and her husband to have been the result of the employment of a soiled vaginal speculum in the hands of a gynecologist. This lesion healed under local treatment and no consequences were noted.

In the year 1875, this patient consulted us again for relief of a cutaneous pruritus which yielded promptly to simple treatment.

On the 5th of May, 1902, she again sought relief, and on this occasion complained of certain facial lesions the unsightliness of which distressed her. She was now fifty-seven years of age, and had been living in a home surrounded by all the luxuries which large wealth commands. Some weeks before the consultation, she had suffered from an enervating fever, to the weakness resulting from which she referred her trouble. During the preceding month, she had not been living in a moist atmosphere; and had been, on the advice of her family physician, resting as quietly as possible during the most of the day in a reclining chair.

When examined she was found to have an enlargement of the thyroid gland which had attained the size of a small orange. There was marked exophthalmos, classical tremor, great weakness, and some inappetence. Her pulse was 110 to the minute, soft, compressible, and full; there was no murmur either cardiac or vascular. Her color was a dull gray, her mind active, her intelligence (always of a high order) unimpaired. On the slightest exertion she became much prostrated.

The skin of her face was continually moistened with sweat, and the seat of a score or more of vesicles chiefly clustering over the brow, nose, cheeks, and chin. These lesions were elevated, flattened to obtuseness, pea-sized, tense, very well defined, discrete, unaccompanied by signs of inflammation, and occurring in no other region than the face. When punctured, they gave exit to a clear fluid having the color of sweat. When unruptured, some of the larger lesions suggested boiled sago-grains; a few had a dull opalescent hue, others were very slightly empurpled; at a distance, the color was almost that of lead. The relics of a few desiccated lesions, shreds of torn blebs and very ill-defined mottlings of the surface, could be detected.

The lesions, single and in totality, were identical with the symptoms of hidrocystoma ably studied and described by Robinson. We have had an interesting group of cases with exactly similar cutaneous lesions upon the face, in laundresses applying for relief at the clinic, many of whom had been sweating when enveloped in the moist atmosphere surrounding the laundry-tub. The social position of this patient forbade a biopsy of the elements of the eruption.

Case II. *Exophthalmic Goitre and Telangiectases.* Miss N. M., aged twenty-four years; family history good; had bronchopneumonia at two years; scarlet fever at eleven, with no untoward sequelæ; diphtheria at fourteen, and measles at twenty-one. Menstruation began at thirteen, and has been practically normal except for occasional dysmenorrhœa. She gives no history of pelvic trouble.

The patient had goitre at twelve years, after a severe sore throat; and the gland has remained of about the same size since the beginning of the disease, increasing in volume slightly during "colds." She taught school from seventeen to twenty-four years of age, and does not think she was especially nervous during this time as the result of the strain. About two and a half years ago she was greatly worried over the sickness of a brother ("blood poisoning"). There is no history of alcoholism.

Two years ago the patient noticed a marked redness of the skin over the right frontal eminence; this gradually spread over the forehead. At this time she began to have cardiac palpitation on exertion. There were no other subjective symptoms except weakness in the legs. She said she felt "as though her knees would give out under her."

On examination, she is seen to be poorly nourished, of sickly appearance, and of slender build. Her weight is 112 pounds. The forehead shows a diffuse redness extending to the roots of the hair. On close inspection a fine network of vessels is visible throughout the area, at some points more numerous than at others. Pressure under a glass shows new vessel-formation, with small scattered areas of brown pigment deposits. The redness extends over the cheeks and angles of the jaws to the neck, especially on the left side, where it appears as a tongue-like prolongation over the enlarged left lobe of the thyroid. Part of the red-

ness disappears if the patient remains perfectly quiet for a brief time. New vessels, however, are present over the frontal eminences, the prominences of the cheeks, and over the lobe of the thyroid. The eyes show normal reflexes. Von Graefe's, Stelwagon's, and Möbius' signs are absent. There is a very slight exophthalmos. Circumference of neck measures 29½ cm. Both lobes and the isthmus of the thyroid are moderately enlarged, the left showing greatest change; the gland is soft and not sensitive. The lungs are normal; the heart is normal in size; there are no murmurs; the cardiac pulse is 130 per minute (while the patient is quietly resting), regular and forcible; a murmur is present over the right side of the neck; there is no unusual cervical pulsation. The abdomen is normal; the pelvic organs were not examined. There is no œdema. There is a well-marked tremor in the outstretched hands. All the reflexes are greatly exaggerated. The urine is negative. There are no red or brown patches on body; the skin is moist and irritable.

Case III. *Cutaneous Pruritus in Exophthalmic Goitre.*—Mrs. J. C., aged forty-two years. Her family history is good; her personal history satisfactory until recent years. Goitre has been present twelve years. Five years ago her health began to fail; there was great palpitation and dyspnœa, with general body weakness. Three years ago cutaneous symptoms began; the skin became irritable; itching at times was intolerable, and the patient constantly excoriated herself in efforts to relieve the pruritic symptoms. Examination showed both lobes of the thyroid enlarged and soft; the heart was normal in size; no murmurs; pulse, 120 to 140, regular; exophthalmos, tremor; urine negative. The skin of the face and of much of the body was reddened, and presented many small, scattered, and torn papules.

Case IV. *Cutaneous Pruritus and Angioneurotic Œdema in Exophthalmic Goitre.*—Mrs. A. C. J., forty-nine years of age, a widow and mother of two healthy children, had been under the care of a distinguished member of the profession for sixteen years. She had passed the climacteric at forty-six. The full history of the exophthalmic goitre from which she suffered for a large part of this time appears in the records made by her physician. He consulted one of us on February 27, 1899, in consequence of a complicating cutaneous disorder.

The patient was found in bed, pallid in color, with a goitrous enlargement of the size of a large apple, exhibiting marked exophthalmos, having an exceedingly rapid, weak, soft pulse, and showing distinct tremor. Some few weeks before, tubercle bacilli had been recognized in the sputum. She had a slight bronchial cough and dulness on percussion at the pulmonary apices; the skin was for the most part dry. Her treatment for some weeks before had been by internal administration of strophanthus, pilocarpine, and strychnine; with absolute rest and a diet strictly limited to milk and the cereal known in this country as "popcorn." It was a question whether this last had in any way contributed to the cutaneous symptoms, but inasmuch as the latter persisted for some time after the withdrawal of this cereal from the dietary, a causal relation between the two may be doubted.

When examined, the skin was found to be the seat of excessive itching and burning, decidedly most annoying over the lower limbs and the hips, preventing sleep at night and greatly disturbing the digestive processes. In many places the surface was excoriated in attempts to relieve the pruritus by scratching and rubbing. Giant wheals both actively

developed and relics of a former activity in the shape of vivid and dull reddish macules were evident here and there over the surface, especially upon the hips. Complaint was made that in all positions in the bed the skin of these parts gave the patient much distress.

Elsewhere over the body, in trifling measure upon the face and neck, there were pruritic symptoms, evanescent rosy blotches and ill-developed wheals.

By the end of the following month the patient was relieved of the local symptoms by employment of the simpler methods of treatment, including the protection of the surface by the Pick dressing. At the present date the patient is living and has survived a fracture occurring as an accident when ascending the stairs. Her improvement in the diminution in the size of the goitre and the exophthalmic symptoms are unquestionably due to highly scientific management by her physician who has been from the first in charge of her case.

Having in view the instances herein reported and surveying the literature devoted to the special facts which they illustrate, it is clear that important lesions of the skin, some involving serious structural change in the corium and subcutaneous tissue, may coexist with exophthalmic goitre. About one hundred and eleven reports have been made of cases of this character, the list including, first, about forty-nine cases of hyperidrosis; next, each in equal frequency, fifteen of pigmentary changes and myxœdema; about fourteen cases of simple œdema of the skin; five cases of scleroderma, most of them generalized, a small portion representing the circumscribed form; then alopecia, often generalized, and vitiligo; lastly, one or two instances each of telangiectasis, purpura, urticaria, erythema, and one only (that herein reported) of hidrocystoma. Among the accidents of the same morbid process, most of them evidently rare, are hemorrhage from the skin, bronzing of the integument, eczematous and erysipelatous accidents, and localized anæsthesia.

The affections thus catalogued can for the most part be readily assigned to one of the three groups described in the introductory paragraphs of this paper. Thus, for example, it is safe to assume that some of the cases recorded as eczematous, urticarial, erythematous, etc., were either accidental concurrences in the general disorder or were remote reflex disturbances due to irritation of the nervous centres. Again, the marked frequency of hyperidrosis in the list of cutaneous symptoms points unerringly to the vascular disturbance which is so fixed an element in the nosology of exophthalmic goitre, and which it is barely possible may be in turn responsible for the frequency of pigmentation after the existence of the malady for a long period. The intimate relationship existing when such disorders as scleroderma and myxœdema accompany or, as may be the issue, succeed the common signs of Basedow's disease is obvious.

With reference to the patients whose cases are described above, Cases III. and IV. may be referred to the first or second group defined herein,

that in which the cutaneous symptoms are either accidents of the general process, or possible surface indications of the mischief beneath the surface.

With Cases I. and II. there is a marked departure from the limits established for the first group. In a single instance (that of Case I.) the exanthem may be regarded as distinctly though remotely the result of one of the prime symptoms of the general disease. In the other (Case II.) there is a new formation of vessels apparently as the immediate result of the evolution of the malady.

Respecting the first case, that of hidrocystoma complicating exophthalmic goitre, a careful survey of literature has failed to discover any other case. Hyperidrosis, however, a condition in close causal relation to hidrocystoma, as already shown, has been frequently observed. So commonly, in fact, does sweating occur, that it may almost be expected as a symptom in Graves' disease; one of the manifestations of the profound vasomotor instability found in that malady. Dreschfield[2] observed profuse sweating in forty cases, occurring by day as well as by night, most marked in those presenting the most serious symptoms of the general disease. Watson-Williams[3] records a case in which the hyperidrosis affected principally the right side. It is interesting to note also that in this patient von Graefe's sign, dilatation of pupil and enlargement of the thyroid were most pronounced on the right side. Excitement would be followed by profuse sweating of the right leg below the knee. Hector Mackenzie[4] comments on the frequency of hyperidrosis, especially of the palms, and reports several cases. Others have made similar observations. Occasionally, where certain complications have existed, hyperidrosis has not occurred and the skin has been found to be dry.

A special interest, from the point of view of the dermatologist, attaches to the case of hidrocystoma here reported because of the conditions in which the vesicles formed. Robinson has called attention to the circumstance, amply corroborated in our clinical experience, that the special factors of the disease are, first, profuse sweating; second, environment in a moist atmosphere, such as that in which most laundresses labor. With these favoring conditions, it is found that the subjects of the disorder are mostly women and these in middle life or more advanced years, doing work in the summer months. Robinson states, however, that he has observed the disease also in cooks, and indeed in persons who have neither been cooking nor washing. Once only the symptoms occurred in a man twenty-eight years of age, and then upon one side of the nose only. The observation here recorded is of special interest as showing that hidrocystoma may develop in classical symptoms upon the face of a woman in nowise exposed to a moist atmosphere, and doing no work of the kind middle-aged women often

perform. Briefly, it is shown that cardiac and vasomotor disturbances in exophthalmic goitre are capable of inducing the characteristic lesions of the disease. The pathology of the lesions and their relation to the excretory duct of the sweat-gland at some point in the corium has been thoroughly established by Robinson's demonstrations.

With reference to the second case herein reported, it may be said that hyperæmia of the skin is of common occurrence in Graves' disease, as can readily be explained by the irritability of the vasomotors so constantly present. The intercurrence of telangiectases of the skin, however, is very rare. The writers have been able to find but one reported instance. Létienne and Arnal[5] record the case of a woman (Graves' disease) who presented multiple telangiectasic areas over the entire body. The patient was twenty-seven years old, with a family history showing a decided nervous taint. Her personal history was also bad—hysterical crisis at twelve; rheumatism at fifteen; menstrual and digestive derangements. At twenty-six she noticed a small red spot over the sternum; similar macules appeared elsewhere, and one year later examination disclosed the following: round and oval, scarlet to dark red spots, of variable size (not exceeding the diameter of a 50-centime piece), disseminated without order over the entire body, the shoulders and neck excepted. The spots show a dark centre surrounded by a fine network of vessels with arborizations, gradually losing themselves in the surrounding skin; they disappear on pressure; there is no desquamation; two larger areas are present above the malleoli, painful on pressure; no spots on the mucous membrane. The right lobe of the thyroid is hypertrophied. The pulse is regular, 105; no exophthalmos; marked tremor, and great nervousness.

After a period of treatment the patient seemed to improve, though new spots had appeared and none of the old had disappeared. In this case there was a possible etiological factor in alcoholism, of which the patient gave an obscure history. The reporters of the case, however, think the condition to be one of nervous origin.

Although Osler[6] speaks of pruritus as an occasional symptom in Graves' disease, and reports a case in which it constituted a severe and persistent complication, medical literature is singularly devoid of recorded instances in which this cutaneous symptom was prominent.

Greater interest attaches to the subject of œdema in its various forms as associated with exophthalmic goitre. Numerous cases are reported, and the discussion, which is always full, leads by natural and logical sequence to a consideration of myxœdema and scleroderma as related to Graves' disease. Some degree of œdema is present in a large proportion of all cases. It varies in its nature and location. It may be persistent or fleeting; pitting or non-pitting; symmetrical or non-symmetrical; with and without albuminuria. The hands, eyelids, face and

neck, ankles and legs are common sites. Maude[7] has divided the œdema of Graves' disease into three classes: (*a*) from cardiac insufficiency, generally in severe cases; the œdema may appear suddenly and become general; (*b*) of nervous origin; slight swelling of instep and lower legs, without cardiac insufficiency and albuminuria; (*c*) transitory œdema; irregular, unsymmetrical, lasting but a few hours; the arms, hands, neck, and face are usually selected. This class suggests a type of œdema analogous to or identical with that found in giant urticaria; which skin lesion is mentioned by Möbius[8] as occurring in Graves' disease. Maude's classification would seem to be somewhat deficient, as in it no place is found for œdema of renal origin nor for the brawny infiltration (mucoid) which is present when myxœdema is a complication. Hector Mackenzie[9] writes that it is common to find œdema of dependent parts in debilitated subjects of Graves' disease from gravity and an enfeebled heart action, and quotes Basedow as having seen in emaciated patients swelling of the joints and tissues of the abdomen, as well as non-pitting œdema of the legs. He reports seven cases of œdema of the eyelids, in three of which the condition persisted after recovery; two of œdema of the legs, one of which showed persistent albuminuria after disappearance of the swelling; and two cases of persistent, probably mucoid, infiltration of the connective tissue of legs, suggesting myxœdema. Vigouroux[10] has expressed the opinion that the swelling of the eyelids is not always true œdema, but rather a condition due to paresis of the orbicularis muscle. Dreschfield[2] noted transitory œdema in several of his cases, and in Watson-Williams'[3] case œdema of the legs was the first symptom noted.

The relation of Graves' disease to myxœdema is one of exceeding interest, and inasmuch as the condition of the skin and subcutaneous tissues plays an important role in the diagnosis of the latter, a consideration of the relation between the two diseases comes properly within the scope of this paper. A number of cases have been observed in which exophthalmic goitre has been followed gradually by myxœdema, with all the cutaneous changes which attend that disease. Kowalewski[11] was among the first to report an instance; an epileptic, with well-marked symptoms of Graves' disease, showed, after a paroxysm, swelling of the feet, legs, and face (character of swelling not given). Later mental hebetude developed. He considered myxœdema as an expression of a severe type of Graves' disease. Sollier[12] reports a rather peculiar case in which the myxœdematous (?) symptoms developed first. The patient suffered with pains in the hand. These became swollen, the swelling gradually extending over the entire body. Later the symptoms of Graves' disease came on. When seen by Sollier there was swelling of the entire body, *atrophy* of the thyroid, nervous irritability, exophthalmos, tachycardia, tremor, pigment flecks over body. Under electrical and

hydrotherapeutic treatment all symptoms of myxœdema and nearly all of Graves' disease disappeared. One is not fully convinced that in this case myxœdema was present. In von Jaksch's[13] case typical symptoms of Graves' disease were present; the patient also showed a non-inflammatory, non-pitting swelling of both legs, which gave the impression that some substance more resistant than water was deposited in the subcutaneous tissues, suggesting strongly myxœdema. Williams' case[14] was that of a woman of thirty with Graves' disease, treated with arsenic and change of climate, recovery following. Five years later she became languid; the face, arms, and hands were puffy; there was no albuminuria. Myxœdema was diagnosticated, and recovery followed the use of iron and arsenic. The same year Joffroy and Achard[15] published a case of a woman of twenty-three who presented at first the picture of Graves' disease; later, the goitre and exophthalmos disappeared; she became very weak; œdema of the feet, legs, body, and face developed; there was great mental apathy; death followed, and the autopsy revealed hyperplasia of the connective tissue of the thyroid, with disappearance of parenchyma. Putnam[16] reports a case in which the existence of Graves' disease is somewhat uncertain. A woman of fifty-five years, in whose family myxœdema had occurred twice, developed typical myxœdema, with usual skin changes. This, however, was preceded by two symptoms of Graves' disease, struma and tachycardia. Under thyroid treatment recovery ensued. Four cases are reported by Baldwin:[17] (1) A boy of ten years, sluggish, overgrown, mentally dull; skin dry, harsh, inelastic, and puffy; at six years he had heart trouble, pronounced at the time to be Graves' disease; recovery occurred under thyroid treatment. (2) A girl of fourteen years with typical Graves' disease; six years later a typical myxœdema; improvement under thyroid exhibition. (3) A girl of fifteen years with tachycardia, exophthalmos, tremor, goitre; after six years; mental hebetude, intolerance of cold, poor circulation; skin dry, harsh, inactive; cured with thyroid extract. (4) Woman of forty-four years; nervous history; Graves' disease for four years; later, mental hebetude, intolerance of cold, melancholia; skin harsh and dry, face swollen; cured with thyroid extract.

Loew[18] considers the œdema of nervous origin to be myxœdematous or premonitory of myxœdema. He reports two cases: (1) A woman of twenty-three years, with typical symptoms of exophthalmic goitre; in addition, pigment spots everywhere present, with patches of vitiligo at elbows and knees; the lower part of the legs swollen; skin hard, tight; very slight pitting; the dorsum of the feet not affected. (2) A woman aged twenty-four years, with Graves' disease; the lower limbs from middle of thighs to dorsum of foot swollen, hard, inelastic, non-pitting. A case of Gautier's[19] is reported briefly. In 1894, Graves' disease; im-

provement; in 1895, recrudescence; improvement; in 1898, myxœdema; hard, fibrous thyroid; improvement under thyroid treatment.

Pasteur[20] reports the case of a woman of sixty-five years who developed Graves' disease twenty years before (1878). In 1886 she presented typical symptoms; under observation the enlarged thyroid became atrophic (effect on pulse rate not reported); in 1893 the patient had permanent bradycardia (30–55), cardiac dilatation, apathetic face, altered voice, sensitiveness to cold, and clumsiness of fingers. Oncoming myxœdema was predicted. Death occurred in 1900, preceded by extreme cardiac insufficiency. At the autopsy, marked sclerotic changes were found in the thyroid.

Hirschl[21] discusses the relation between Graves' disease and myxœdema, and reports the case of a woman of thirty-three years, with fairly good history. In August, 1899, symptoms of exophthalmic goitre developed, following a fright; in October palpitation became less, mental hebetude developed, the thyroid became dense, the legs became swollen and hard, and the skin of the face thickened. The left leg was increased in size, smooth, non-pitting, reddish-brown in color; the swelling ended abruptly at the ankle. The right leg was similarly but less extensively affected.

The close pathological relationship existing between myxœdema and scleroderma has been shown by Jeanselme,[22] Singer,[23] and Hektoen.[24] It is not surprising, therefore, in view of what has been said of the association of myxœdema and Graves' disease, to find that occasional instances of the coexistence of scleroderma and exophthalmic goitre are recorded. Grünfeld,[25] in 1896, found three cases in literature; the first by von Luebe in 1875, the second by Kahler in 1888, and the third by Jeanselme in 1895. He himself reports the fourth case. A woman with well-developed Graves' disease was attacked later with scleroderma of moderate severity; a cure was effected with thyroid extract. Osler,[26] in a masterly article on scleroderma, mentions one case associated with Graves' disease. A man of forty years suffered from exophthalmic goitre for two years; the symptoms were typical; scleremic changes then developed in the skin of the legs below the knees. He also records two cases in which tachycardia was present. He found in reviewing the reported cases of scleroderma treated with thyroid, that of ten cases two were cured; seven were improved more or less; and one was not benefited. Dupré and Guillian[27] report a case in a woman of thirty-three years; goitre appeared at thirteen years; exophthalmos at fourteen years; later a clear symptomatology of Graves' disease was recognized; the signs of scleroderma developed at twenty-four years; the hands, forehead, and nose were affected. This patient was of decidedly neurotic type.

Pigmentary changes in the skin have been frequently observed.

Vitiligo is mentioned by Rolland[25] in his thesis as occurring in exophthalmic goitre. Raynaud[29] reports a number of cases. Marie[30] records a case of generalized vitiligo, with areas of brown pigmentation. His description of the spots on the thighs suggests possible telangiectases. Lucy[31] reports a typical case of Graves' disease in which extensive patches of leucoderma were present, as well as areas of brownish pigmentation. The vitiligo began several months before the general disease, but increased greatly during the course of the latter. In this case there was an evident distribution of the patches along the course of the ulnar nerve. Campbell[32] observed a similar combination of leucoderma and melanoderma in three cases of Graves' disease. In all there was a tendency to bilateral symmetry. The pigmentation of the skin may be localized or diffused. Perry[33] reports an interesting case of a woman with exophthalmic goitre who presented a diffuse generalized pigmentation of the skin. There were no evidences of Addison's disease, and under treatment, extending over a period of several months, the bronzing disappeared almost entirely. Burton[34] records a case with pigmentation of the face, neck, axillæ, back, and genitals; Graves' disease was present, but Addison's disease was not excluded. Drummond[35] mentions six cases with localized pigmentation; one showed areas of leucoderma also. Nichols[36] saw a woman and Dore[1] has reported pigmentation and purpura in two different patients, with exophthalmic goitre, in whom large pigmented areas appeared. When Addison's disease is associated with Graves' disease, as in the case of Kruella's,[37] the pigmentation, rather than an anomalous, becomes a cardinal symptom. Other trophic changes have been noted. Among these alopecia is common. Yeo[38] saw a case in which there was falling of the eyebrows, at first unilateral, corresponding to the side presenting the goitre and exophthalmos; later both sides were affected. Barnes[39] reports a case with universal alopecia. Smith,[40] one with general alopecia and glycosuria. In the fifteen cases observed by Mackenzie[9] five showed alopecia in varying grades.

Other dermatoses to be mentioned are urticaria, reported by Bulkley[41] and Rolland;[28] and eczema, observed by Zeleneff.[42] Gangrene of the skin has also been recorded.[28]

In a contribution to the general subject under discussion, where the cutaneous syndromes of exophthalmic goitre have been chiefly considered, the questions of moment respecting the etiology and pathology of Graves' disease may be left to the investigators in the field of inner medicine. At this time it will serve no useful purpose to inquire with scientific precaution into the value of the theories of origin of exophthalmic goitre; whether, for example, there is in these cases a hyperthyroidization; whether there is a primary change in the nervous

centres radiating to the thyroid gland; or whether the gland itself first secretes a toxin, which later acts as an irritant to the nervous centres. By post mortem examinations as well as biopsies of the tissues of the organ, it has been made clear that in many cases after a period of morbid activity the glandular tissue of the thyroid is destroyed by a species of disintegration (cystic, collagenous, colloid, etc.), and that after disappearance of the parenchyma there is left chiefly an hypertrophy of the connective tissue. The persistence of many of the symptoms of exophthalmic goitre after such complete destruction of the secretory tissue of the gland, would militate against the theory of continuous intoxication of the system from that source.

The influence of the nervous centres and nervous tracts in the production of such cutaneous symptoms as the *tache cérébrale* or the lesions of herpes zoster is fully recognized. The established co-existence, in certain cases, of scleroderma and exophthalmic goitre if common etiological factors can be demonstrated for the two, would point to their nervous origin, seeing that the circumscribed (morphœa) type of scleroderma is often displayed in lesions distributed along a single nerve tract; and in the generalized form of scleroderma the early œdematous pitting stage of the disease suggests in a striking manner some of the symptoms of myxœdema, with which disease also, as shown above, exophthalmic goitre is frequently associated. On the other hand the cutaneous symptoms in lepra, though in some instances distinctly traceable to implication of the nerve trunks, as when anæsthetic and hyperæsthetic symptoms can be recognized, may also develop without any alteration of cutaneous irritability to heat and pain, and may thus have their remote origin without question either in the bacilli of lepra or in the toxins of such micro-organisms.

The prime symptoms of exophthalmic goitre are usually enumerated as enlargement of the thyroid gland, exophthalmos, tremor, and tachycardia. Every clinician knows that of these supposedly essential symptoms each in different cases may be wholly absent; so that, notably, a patient with Graves' disease may neither have bulging eyes nor a goitrous swelling. From the point of view of the dermatologist and of the diagnostician, questions of interest arise when, in the absence of one or more of these prime symptoms, dermatoses occur of unusual type or of doubtful origin and relations. Problems of a novel sort would probably be presented to the consideration of a physician confronted with a group of newly formed bloodvessels in the skin of the face, accompanied by distinct tachycardia, without either exophthalmos or thyroid enlargement; and the same would be true if the cutaneous lesions were those of hidrocystoma, or consisted of two or more morphœa patches on the side of the neck, or of an attack of angioneurotic œdema affecting the general surface of the body.

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NOTES ON THE EMPLOYMENT OF EPICARIN IN TINEA TONSURANS AND TINEA CIRCINATA.

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AND

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EPICARIN was brought into notice several years ago by Prof. Kaposi, of Vienna, as a substitute for naphthol in the treatment of certain diseases of the skin. It is said to be a condensation product of creotinic or creasotinic acid and B. naphthol, and to combine the properties of creasote and naphthol.

Epicarin is a reddish amorphous powder with a slight odor resem-

bling acetic acid. It is soluble in alcohol, ether, and liquid vaselin. It has usually been employed in the form of a 10 to 20 per cent. alcoholic or soda solution, or in the form of ointment of the same strength.

Kaposi employed it at first in the cure of scabies. Eighty cases were treated with excellent and rapid result. He also employed it in a certain number of cases of ringworm, and in prurigo of children with similar good results. In eczema and psoriasis it is said to have proved irritating.

Pfeifenberger found that where much dermatitis was present with scabies, epicarin proved somewhat irritating. In 7 per cent. ointment form he found that the scabies could be cured, but that the attending dermatitis required more soothing remedies.

Pfeifenberger employed epicarin in the case of children, from one to fourteen years of age, without finding any untoward effect upon the kidneys, such as sometimes accompanies the use of B. naphthol. In scabies the severe itching diminished after the first or second inunction, in most cases; the skin, however, became red, dry, and rough, showing superficial fissures here and there.

To prevent irritation of the skin in the treatment of scabies, the epicarin was stopped after having been used every night for three nights, and a soothing ointment, such as ung. diachylon, was applied for several days. Then a bath was ordered. This carried off the superficial scaly skin and with it the itch mites. No application was made for three or four days, at the end of which time, if any spots showed disease, fresh inunctions of epicarin were employed. Five or six generally proved sufficient.

The treatment completed, the skin presented a smooth, soft texture with a shiny aspect and a reddish color. This staining or coloration lasted for some time after the cessation of the treatment. It may be mentioned that the epicarin treatment was applied immediately, no bath preceding treatment.

The maximum length of time required for a cure was not more than nine days, the delay being caused by the concurrent dermatitis, which had to be handled carefully. Prurigo in children was likewise treated by epicarin with excellent effect.

In addition to the 10 to 20 per cent. alcoholic solution of epicarin the following ointment, chiefly employed in the scabies cases, was used:

℞—Epicarin	7	grm.
Cretæ albæ	2	"
Vaselini albæ	30	"
Lanolin	15	"
Axungiæ porci	45	" —M.

The material employed in our investigations was derived chiefly from the out-patient department of the Children's Hospital of this city, and was subject to the vicissitudes usually experienced in such clinics. The solicitude shown by the parents, whose children were deprived of

school privileges during the presence of ringworm on the scalp or body, fortunately afforded us more opportunities for following the course of treatment than are usually permitted.

After examination and diagnosis of each case, the hair was clipped or shaved around the neighborhood of the patches, or in some cases, where the disease was diffuse, the entire scalp was shaved. The scalp was then carefully gone over and the tincture of epicarin was vigorously rubbed into every suspicious patch of skin. The parent was provided with some of the same tincture, or in some cases with the ointment, and was told to rub it well into the scalp wherever any diseased spots could be found, once or twice daily. In some cases a germicide soap was also employed to shampoo the scalp daily, in order to prevent the accumulation and diffusion of dry scales containing the ringworm fungus.

In all cases thus treated the personal equation of the nurse or attendant counts for very much. We found that the few cases treated in the hospital wards by skilled and intelligent nurses were cured much more rapidly than those committed to the hands of less intelligent mothers for home treatment. Even here, however, it was found that the greatest difference in results obtained between intelligent and anxious parents and those who were lazy and indifferent.

The number of cases, though much greater in total than those reported, was still insufficient to allow the employment of a great variety of preparations of the drug. We mostly used the preparations as described by Kaposi; that is, the 10 and 20 per cent. tincture and ointment. The tincture seemed decidedly the most efficient preparation. Used in the ward cases immediately after depilation the effect was surprising. In one very recent case a cure was effected within ten days. On an average, five weeks were required to bring the disease to an end.

Although few microscopic examinations were made, it is believed that in each case the fungus involved was the large-spored variety, and that no cases of the small-spored and more inveterate form of fungus came under treatment during the period of our investigation.

Only a few cases of scabies came under observation, and of these only two were treated with epicarin. The formula used was that of a simple 10 per cent. ointment with a base of petrolatum. The result was quite unsatisfactory; the ointment irritating the skin quite severely and not producing much impression upon the disease nor giving much relief from the accompanying pruritus. On changing to the ointment of naphthol and sulphur as usually employed in the skin clinic of the Children's Hospital, very speedy relief was experienced. It is possible that if the compound epicarin ointment, as given above, had been employed, somewhat better results might have been obtained. The old treatment, however, is so satisfactory that it seems hardly worth while to try epicarin further in the treatment of scabies.

TABLE OF CASES TREATED WITH EPICARIN.

Case.	Duration.	Description.	Treatment.	Remarks.	Result.
1	3 wks.	Tinea tonsurans. Two lesions on scalp, half-dollar size, covered with short hairs with an ash-like gray appearance.	Tinct. epicarin, 10 per cent.	.....	Improved.
2	3 wks.	Tinea circinata et tonsurans. Two coin-sized patches on scalp, rough nutmeg grater appearance; some hairs broken off short; others, including those in neighborhood of patches, long but pulling out readily; also patches of tinea circinata.	Germicide soap and epicarin ointment, 10 per cent.	Tinct. epicarin, 10 per ct., applied in clinic.	Improved.
3	3 wks.	Tinea circinata et tonsurans. One patch on scalp; most hairs long, but many loose; tinea circinata also.	Germicide soap and epicarin ointment, 20 per cent.	Tinct. iodine had been employed previously, but without satisfactory result; under treatment two weeks.	Improved.
4	6 days	Tinea circinata. Confined to face; chiefly right side; characteristic rings of vesicular ringworm; some dozen lesions in all.	Tinct. epicarin, 10 per cent.	Two visits to the clinic sufficed to cure this case.	Cured.
5	Some months	Tinea tonsurans. Three or four small infiltrated patches on scalp.	Ung. epicarin, 10 per cent.	The ointment was rubbed in daily, while the tinct. epicarin was applied on his visits to hospital; under treatment two months.	Cured.
6	4 mos.	Tinea tonsurans. Well-marked case; large ash-colored rough patch on back of scalp; irregular patches not so characteristic elsewhere.	Tinct. epicarin, 10 per cent.	Only paid one or two visits.	Improved.
7	3 wks.	Tinea circinata. Three coin-sized patches on scalp and several ring-shaped lesions; tinea circinata of arm.	Tinct. epicarin, 10 per cent.	Epilation was also practised; ceased attendance.	Improved.
8	2 days	Tinea circinata. One lesion on forehead coin-sized.	Tinct. epicarin, 10 per cent.	Treated daily; eruption disappeared in seven days.	Cured.
9	2 days	Tinea circinata. One lesion on knee.	Tinct. epicarin, 10 per cent.	Treated daily; eruption disappeared in fourteen days.	Cured.
10	3 days	Tinea circinata. Several small-ringed lesions on right temple, under chin and on trunk.	Tinct. epicarin, 10 per cent.	Failed to report.	Cured?
11	.....	Tinea circinata et tonsurans. Large oval ring on left leg above knee; some lesions on scalp.	Tinct. epicarin, 10 per cent.	At the end of seven weeks the lesion on knee was reported well; it had probably been so for some time. The scalp lesion was nearly well at the end of ten weeks.	Cured.
12	11 mos.	Tinea tonsurans. Three or four coin-sized patches and a large number of smaller patches in scalp.	Tinct. epicarin, 10 per cent.	The epicarin was applied three times weekly after epilation at clinic, and at home daily; duration six weeks.	Cured.
13	1 mo.	Tinea tonsurans. One coin-sized incipient patch on left side scalp, also a patch of "alopecia areata."	Tinct. epicarin, 10 per cent.	At the end of four weeks seemed well.	Cured.
14	.....	Tinea circinata. Very marked eruption, chiefly over face, neck, arms, legs, and body; lesions ringed.	Tinct. epicarin, 10 per cent.	After several days' treatment decidedly better; patient disappeared.	Cured?
15	.....	Tinea circinata. Distinctly ringed lesions, chiefly on face and ear.	Tinct. epicarin, 10 per cent.	After several days' treatment decidedly better, ceased attendace.	Cured?
16	1 week	Tinea tonsurans. Coin-sized lesion on scalp.	Tinct. epicarin, 10 per cent.	....	Improved.

Case.	Duration.	Description.	Treatment.	Remarks.	Result.
17	1 week	Tinea tonsurans. Small patches on scalp.	Tinct. epicarin, 10 per cent.	.....	Improved.
18	3 mos.	Tinea tonsurans. Scalp pretty well covered with large and small patches.	Tinct. epicarin, 10 per cent. Ung. epicarin.	The scalp was shaved and tincture was applied thrice weekly at the hospital, the ointment being applied at home daily; duration of treatment two months.	Cured.
19	2 wks.	Tinea circinata et tonsurans. Palm-sized patch over right ear, and smaller one on top of scalp.	Tinct. epicarin, 10 per cent. Ung. epicarin, 20 per cent.	Shaved; salicylic colodion to face lesions; afterward ung. epicarin; tincture to scalp; under treatment six weeks.	Improved.
20	1 mo.	Tinea circinata. A single ring-shaped lesion on nose and adjacent skin.	℞.—Epicarin, gr. v. Ung. zinc oxid., ʒiv.	Treatment about a week.	Cured.
21	3 wks.	Tinea circinata et tonsurans. Lesions on chin, face, and scalp.	Tinct. epicarin, 10 per cent.	Treatment three weeks.	Cured.
22	2 wks.	Tinea circinata et tonsurans. Two patches on scalp, one over right eye.	Tinct. epicarin, 10 per cent.	The patch over right eye was well in two weeks; the scalp in three months.	Cured.
23	3 mos.	Tinea circinata et tonsurans. Quite extensive; nutmeg grater patches on scalp.	Tinct. epicarin, 10 per cent.	This case was severe and extensive, but was nearly cured at the end of three months.	Improved.
24	2 mos.	Tinea circinata et tonsurans. Small, round, elevated patches on scalp.	Tinct. epicarin, 10 per cent.	At the end of two months healthy hairs growing everywhere.	Improved.
25	.....	Tinea tonsurans. Two coin-sized superficial patches on scalp.	Ung. epicarin, 20 per cent.	At the end of three weeks practically well.	Cured.
26	2 mos.	Tinea tonsurans. Well-marked tendency to crusts.	Ung. epicarin, 20 per cent.	The ung. epicarin was said to have produced pustules; however, it was continued and the tincture used on visits to hospital: in seven weeks practically well.	Cured.
27	.....	Tinea circinata. Vesicular ringworm of wrist, smaller lesions elsewhere.	Tinct. epicarin, 10 per cent.	When the tincture of epicarin seemed too irritating an aristol ointment was used for a short time.	Cured.
28	.....	Tinea tonsurans. Light, thin hair; extensive scaliness through scalp; tendency to round patches.	Tinct. epicarin, 10 per cent.	Under treatment five weeks.	Cured.
29	.....	Tinea circinata. A single lesion two centimetres in diameter on right wrist.	Tinct. epicarin, 10 per cent.	At first seemed to increase in size, but soon began to improve rapidly; under treatment three weeks.	Cured.
30	3 wks.	Scabies. Three weeks' duration; well marked on body and limbs.	Ung. epicarin, 10 per cent.	The epicarin ointment was employed for about three weeks; it may have acted favorably, but it proved so irritating that it was changed for a naphthol and sulphur ointment, which acted more satisfactorily	
31	2 wks.	Scabies. Well marked; hands and arms chiefly affected.	Ung. epicarin, 10 per cent.	The epicarin seemed irritating and not very effective; probably recovered under use of naphthol and sulphur ointment as used by 30.	

The conclusions we have reached are as follows:

1. In epicarin we have an important addition to the means of combating ringworm of the scalp. Used, preferably, in the form of a tincture of 10 to 20 per cent. strength and after epilation it appears to act more rapidly than any of the remedies heretofore employed, in restoring the hairs to a normal condition.

2. In ringworm of the body the tincture seems to be irritating and slow in action. The ointment acts better, but is not equal to the ammoniated mercury ointment, nor to most of the remedies ordinarily employed.

3. In (a single case of) favus the result of the use of epicarin was such as to encourage trial.

4. In scabies, so far as our experience goes, epicarin in the form of the tincture and simple ointment is apt to prove very irritating, and is by no means equal to the sulphur and naphthol nor to the other ointments ordinarily employed.

THE BLOOD-PRESSURE REACTION OF ACUTE CEREBRAL COMPRESSION, ILLUSTRATED BY CASES OF INTRACRANIAL HEMORRHAGE.

A SEQUEL TO THE MÜTTER LECTURE FOR 1901.

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Some experimental observations on the rôle played by the vasomotor centre in raising the arterial tension so as to counterbalance the effects of any considerable increase in intracranial tension were presented as part of the Mütter lecture[1] in December, 1901. Since then opportunities have arisen which have made it possible to demonstrate in clinical cases reactions corresponding to those which at that time had only been experimentally produced in animals. To review some of these cases is the purpose of this communication.

It is a well-recognized clinical fact that the rapid[2] encroachment on the intracranial space by a foreign body, of which extravasated blood may be taken as one of the commonest types, is associated with a high tension pulse. Similarly the laboratory experience of many investigators has shown that a transient great rise in blood pressure is an almost uniform accompaniment of artificially induced compression. I

[1] The Mütter Lecture for 1901. The American Journal of the Medical Sciences, September, 1902, vol. cxxiv. p. 375.

[2] In a slowly forming intracranial process, as tumor growth, hydrocephalus, etc., the reactions are inconspicuous, the cerebrum accommodating itself to the gradual increase of tension.

am unaware, however, that any especial interpretation has heretofore been given to this response other than that it represented some aimless or uncontrolled action, from irritation of the vasomotor centre during a certain stage of increase of tension within the cerebral chamber.

The experiments above referred to, which for the most part were carried out upon dogs, tended to show, if the interpretation were a correct one, that this rise in blood pressure represents a purposeful and not a meaningless reaction.[1] The belief was expressed in a regulatory mechanism which controls the rise, and which, under experimental circumstances at all events, is seemingly so adjusted that the vasomotor centre tends to hold the intravascular pressure (arterial tension) at a level slightly in excess of the external (extravascular) pressure exerted by the compressing force against the arterioles and capillary vessels situated in the medulla. In this way a fatal bulbar anæmia, which otherwise would be the result of an equalization of intracranial and a stationary arterial tension, is warded off. Thus, the high-pressure pulse, which characterizes conditions of intracranial hemorrhage, for example, is easily accounted for, and its measured level of tension may be taken as an indication of the degree of circulatory embarrassment from which the medulla is suffering in consequence of the compressing force. It was pointed out that under these circumstances the continuance of respiration hinged upon the efficiency of the vasomotor mechanism in holding the blood pressure at a certain level. Should the vasomotor centre fail to keep the arterial tension in excess of the experimentally increased intracranial tension, the respiration would immediately cease, owing to the anæmia of the centre governing it. Consequently, as will be emphasized in the discussion of some of the following cases, the sequence of events in case of immoderate intracranial tension is, primarily, exhaustion of the vasomotor mechanism with fall in blood pressure, and, secondarily, failure of respiration in consequence of the ensuing bulbar anæmia.[2]

[1] In a note appended to an article by the writer in the Mittheilungen a. d. Grenzgebieten d. Med. u. Chir., 1902, Bd. ix. p. 773, in which this experimental work was reported at some length, one of the editors (Naunyn) states that this rise in blood pressure during compression had been noted and described by himself and Schreiber in their well-known monograph, "Ueber Gehirndruck," published twenty years ago. (Arch. f. experim. Pathol. u. Pharmakol. 1881, Bd. xiv. p. 1.) I regret having made no reference to the contents of this classical paper. As a matter of fact, however, this reaction has been noted by almost all experimenters who have worked along these lines, and the rise in blood pressure on which most stress is laid by these particular writers is that which occurs early in compression, the "primäre Erhebung," which is a result of sensory irritation, and not the subsequent and long-enduring rise from anæmia which we are discussing. The failure to record the degree of intracranial tension on the kymograph alongside of the blood pressure probably explains why previous observers have failed to recognize what seems to be the true significance of the rise in blood pressure. Prof. Naunyn expresses some doubt as to the correctness of the interpretation which was offered, namely, that of a "Regulationsmechanismus." Future observations will settle the point.

[2] This relationship of the respiratory action to blood-pressure levels and to the degree of intracranial tension was especially well shown in cases in which vasomotor (Traube-Hering)

In the majority of circumstances the vagus centre is likewise stimulated under the effects of compression with the resultant familiar slowing of pulse rate, which, however, does not seem to bear so definite a relation to the degree of increased tension. Aside from the fact of its frequent concomitance the brachycardia does not apparently play any particular part in the reaction under discussion, nor can it be always said that the more advanced the compression the slower will be the pulse rate.

The significance of this vasomotor regulation, should it have been possible to establish it as true for man as well as animals, was fully realized, but, unfortunately, at the time the Mütter lecture was prepared, no opportunity had been offered on clinical cases to satisfactorily corroborate the laboratory findings, much less to put the facts to any practical application.

The introduction for clinical purposes of a simplified form of the original Riva Rocci blood-pressure apparatus has enabled us to take observations on arterial tension, and to plot them on charts which simulate in a useful way the invaluable records which in the laboratory may be obtained by taking blood-pressure records directly from an isolated vessel. By employing this apparatus it has been possible to chart graphically the blood-pressure reaction in several cases of intracranial injury, and thus to bring clinical cases in line with the experimentally induced conditions. The results have proven of such interest and the method of observation of such practical value that it is hoped the few cases, which will subsequently be given at some length, may suffice to further illustrate the points which the experimental work has brought out.

Prof. Kocher,[1] in his recent monograph, has for the sake of convenience divided into several stages the period between the first onset of compression symptoms and the terminal paralysis which may end the story. These stages, corresponding as they do to a given degree of circulatory disturbance consequent on the increase of tension, have individually a more or less characteristic and distinguishable symptom-complex. The process, of course, may come to a standstill in any one of the various stages. Kocher's classification is a most useful one, and inasmuch as the cases, which have been selected, conform with and exemplify the divisions which he has drawn, the latter will be briefly outlined.

waves were called out. Under these circumstances active respiratory action corresponded to the crests of the waves—that is, to *periods of blood pressure exceeding in degree the intracranial tension;* whereas the hollows of the waves during which *the blood pressure fell below the intracranial tension,* with resultant temporary anæmia, invariably corresponded with periods of respiratory cessation.

[1] Hirnerschütterung, Hirndruck u. s. w. Nothnagel's Specielle Pathologie und Therapie, 1901, Bd. ix., Thiel 3, Abt. 2, p. 186.

STAGE I. ("*Compensationsstadium.*") The first stage, that of circulatory compensation, corresponds to an early period or mild degree of compression, during which the encroachment on the intracranial space, by some foreign substance which displaces the normal contents of the cerebral chamber, is not sufficient to seriously compromise the circulation. By the escape of cerebrospinal fluid and by a certain amount of narrowing of the venous channels, the process is accommodated with the avoidance of any pronounced degree of venous congestion of the brain. Under these circumstances symptoms, although not absolutely latent, are in the main insignificant.

STAGE II. ("*Anfangsstadium des manifesten Hirndruckes.*") If the process continues to the point of failure of this circulatory compensation a condition of venous stasis is brought about, with a lessening of the normal amount of blood flowing through the capillaries (Dysdiämorrhysis). At this time symptoms of disturbed cerebral function are inaugurated evidencing an early stage of actual compression—headache, vertigo, restlessness, roaring in the ears, a disturbed sensorium with excitement or delirium, an unnatural sleep, etc. Other symptoms also become outspoken. Among these, of highest importance is the recognition by means of the ophthalmoscope of some distention and tortuosity of the veins radiating from the optic papilla; indeed, a certain degree of venous stasis may have been appreciable in the eye-grounds during the previous stage of compensation. Indications that the venous congestion is influencing bulbar circulation may be apparent as a slowing of the pulse with or without a certain rise in blood pressure.

STAGE III. The third stage, that of advanced compression phenomena ("*Höhestadium des manifesten Hirndruckes*"), corresponds to a condition of capillary anæmia due to a further increase in intracranial tension. This anæmia in case of "local compression" may have exerted its effects primarily over a circumscribed area of the cerebrum, throwing out of function that part of the brain in its vicinity with corresponding paralytic symptoms. Should, however, the pressure from such a local process be sufficiently far-reaching to involve the medulla, or should the medulla from the start have been involved in the threatened anæmia in correspondence with the rest of the intracranial contents (that is, in case of "generalized compression"), then the period of vasomotor regulation follows with its characteristic rise in blood pressure. This reaction may last an indefinite period, until relief is afforded or until an increase in compression is more than can be compensated for, and the terminal stage of compression steps in to supplant it. Associated with the rise in blood pressure may be seen marked respiratory disturbances, which are especially distinctive when the former is accompanied by rhythmic alterations in level. The periodicity of symptoms so often observed during this stage, and refer-

able not only to respiration, but shown also by rhythmic alterations in size of the pupils, by wavering increase and diminution in depth of stupor, and by many other signs indicative of alterations between irritative and paralytic symptoms, is due to this vasomotor rhythm associated as it is momentarily with sufficient cerebral circulation (Eudiämorrhysis) alternating with a period of inadequate or totally deficient blood supply (Adiämorrhysis).

Vagus symptoms are, as a rule, pronounced during this stage, the pulse being slowed to 50, 40, or even fewer beats per minute, but without, or, at all events, with much less apparent evidences of rhythm.

Stage IV. The terminal stage ("*Lähmungsstadium*"), which follows upon an increase of intracranial tension over and above that which can be compensated for by stimulation of the vasomotor centre, is characterized by a falling blood pressure, irregular cardiac and respiratory efforts, deep coma, which supplants the varying degrees of stupor, complete muscular relaxation, wide pupils, broken, snoring respiration, etc., soon to terminate in cessation of all cerebral function, with respiratory paralysis and with the rapid pulse of low pressure, indicating failure of the vasomotor mechanism. An irrecoverable condition of cerebral anæmia (Adiämorrhysis) has been reached.

In this brief characterization of the stages of compression only the main features of the symptom-complex have been cursorily reviewed. In case any one of these stages of circulatory disturbances has been brought about by a compressing force primarily local in origin, the symptoms naturally would vary greatly, from case to case, as the important underlying symptoms referable to the medulla are surmounted by others, called out by paralysis or irritation of those parts of the cortex primarily subjected to the local process. It would not only carry us too far to discuss this superstructure of symptoms here, but be inappropriate, since the cases to follow have been selected to illustrate solely the vasomotor reaction, and it is desirable to avoid as far as possible any complexity in the clinical picture.

These cases are reported from the neurological department of Dr. Halsted's clinic. They may be briefly summarized as follows:

Case I.—Traumatic in origin. One of local compression of considerable degree, not sufficient, however, to compromise the intracranial circulation, and being over a "silent area" of the cortex, giving practically no evidence of its presence. It illustrates the "Compensationsstadium" (Stage I.) of compression with only latent symptoms and no rise in blood pressure.

Case II.—Traumatic in origin. One presumably of general increase in intracranial tension from intermeningeal hemorrhage. It illustrates the beginning period of bulbar involvement (Stage II.), and shows how blood-pressure observations may be utilized as an indication for or against the necessity of operation. The rise in blood pressure

compensated for the compressing force at a relatively low and safe level.

CASE III.—Traumatic in origin. Extensive intracranial hemorrhage progressively increasing until symptoms of the "Höhestadium des manifesten Hirndruckes" (Stage III.) were produced. The indications for operative interference were shown by a steady rise in blood pressure in correspondence with the general increase of compression until a point was reached at which failure of compensation was feared. Symptoms of local compression superimposed on the main underlying ones.

CASE IV.—Apoplectic; also illustrating Stage III. Hemorrhage into the internal capsule. Characteristic symptoms of the supreme reaction of compression with great elevation of blood pressure, indicating the borderland of the paralytic stage. Immediate relief to underlying major symptoms of compression by craniotomy and partial evacuation of clot.

CASE V.—Traumatic in origin. Illustrating Stage IV., the "Lähmungsstadium." A case of fatal compression from intracranial hemorrhage with primary vasomotor and secondary respiratory failure. Operation performed during artificial respiration.

CASE I. (Surgical No. 13,658.) *Compound fracture of os frontalis, with extensive extradural hemorrhage and with no major symptoms of compression; operation.*—The patient was admitted through the accident room on the night of July 31, 1902, with the history of having been struck on the forehead by a six-pound iron hammer three hours previously. He was not knocked down by the blow. There had been no period of unconsciousness, nor had he shown any symptoms whatever of concussion. After his entrance he complained of nausea, and vomited twice. This was attributed to the alcohol he had taken, for he was somewhat inebriated. He complained only of severe "headache."

There was a small lacerated wound near the midline of the forehead, through which a crack in the frontal bone was detected. Beyond this a careful examination was absolutely negative. The eye-grounds were not examined. He was perfectly rational, and had complete recollection of all incidents relating to his injury.

On the following morning his condition was unchanged. He had slept well during the night. His mind was clear, and memory of the events of the preceding night accurate. Examination again failed to reveal any objective symptoms referable to intracranial disturbance. His pulse, respiration, temperature, and blood pressure were normal. The pain in the head was less severe.

Operation, August 1st. Dr. Watts. Ether anæsthesia. After excising the external lacerated wound, exploration of the underlying skull showed a small comminuted and depressed fracture involving both tables. On elevating and removing the fragments a large, underlying, extradural blood clot was brought to view. This hemorrhage was fully exposed by the further removal of bone, and was found to correspond to an area about 7 x 9 cm. in diameter underlying the frontal bone and extending symmetrically on the two sides. It was estimated that about 100 c.c. of extravasated blood was present. The clots were removed with a spoon, the wound washed clean, and a small drain

inserted. The patient's recovery, except for a slight slowing of the pulse for a few days, was uneventful. There was an immediate post-operative relief from the pre-existing headache.

Discussion. The possibility of a considerable narrowing of the intracranial space by an acute process without the production of stereotyped compression symptoms is well exemplified by this case. It is evident that the major or underlying symptoms of compression need not be provoked by an extradural hemorrhage of considerable size if it be in a favorable situation, and, furthermore, that the local pressure effects of the process need not be productive of minor and localizable paralytic or irritative symptoms if they are exerted over so-called silent areas of the cortex. The clot made room for itself by pressing the cerebrospinal fluid out of the cranial cavity and presumably by narrowing the venous radicles in its vicinity without otherwise compromising the intracranial circulation.

An extradural hemorrhage in this situation must needs have been very extensive and under great tension to have transmitted its effects without any associated concussion, to so remote a situation as the bulb, thus causing a slowed pulse and rise of blood pressure. Being over the frontal lobes, moreover, it failed to give appreciable symptoms indicating local disturbance of cortical areas, such as would have been present had the clot formed, for instance, over the motor territory. No psychic symptoms were detected. The circulatory disturbances of the brain due to the pressure of the foreign body and doubtless occasioning a certain amount of anæmia in its immediate vicinity over the frontal lobe were not sufficiently far-reaching to involve any important centres. Possibly had an examination of the fundus been made some degree of stasis might have been made out in the eye-grounds. The pain and headache complained of were practically the sole symptoms, and were undoubtedly of dural origin. In the lower animals especially is the dura found to be a most sensitive structure. Even under anæsthesia an attempt to strip away the membrane from the skull during experimental procedures on dogs will cause pronounced irritative symptoms. Clinically an extradural hemorrhage plays the same rôle, and may be productive of the most severe dural pain and headache. It is interesting to note in this connection that should individuals have headache after extirpation of the ganglion semilunare the pain, in my experience, at least, is invariably unilateral, and referred to the unoperative side, where the dura retains its sensation. In this case, as is usual, the headache was immediately relieved by the removal of the clot.

Among our recent series of cases of cranial injury, in no other instance has a moderate degree of compression been present, uncomplicated by symptoms of concussion. Hence, this case has been chosen

to illustrate the compensation stage. Several cases of fracture of the base with intermeningeal hemorrhage and slight increase of intracranial tension, as told by lumbar puncture, have been seen and found likewise to be unassociated with bulbar symptoms. The element of concussion, however, has always been present in these cases, and has more or less obscured the symptoms which the compression alone might have caused. This combination of pressure factors will be considered in the following case:

CASE II. *Simple fracture of the base; concussion and mild degree of compression from intermeningeal hemorrhage; lumbar puncture; no operation.*—The patient was admitted through the accident ward, April 12, 1902, with the history of having been struck under the jaw two hours previously by a swinging, heavy, steel rail. The blow felled him to the ground, with momentary loss of consciousness.

The note, made on admission, reads as follows:

"A powerful working man, with a large head, a strongly developed lower jaw and facial bones. He lies in a stuporous sleep most of the time, with occasional interruptions of active restlessness. He can be aroused somewhat by the infliction of pain (supraorbital pressure), but will not respond to questions, and relapses immediately into his previous somnolent condition.

"His pulse is 69, regular, and of fairly high tension to palpation. The arterial pressure at the brachial measures 160 mm. of Hg. The respiration is deep, regular, and 24 to the minute. The temperature is subnormal, registering 97° per rectum. On the left side of the chin below the mental prominence is a small, contused, bleeding wound. No fracture of the powerful inferior maxilla can be made out. The jaw can be moved in all directions, apparently without pain. Pressure on the chin, however, causes the patient to wince, apparently from transmission to the skull. The right margin of the tongue has been almost bitten through. There is considerable bleeding from the right ear. Pressure over the supramastoid ridge on the right side gives evidence of great tenderness. There is no bleeding from the left ear or apparent tenderness anywhere on that side of the head.

"The pupils are equal, contracted to a diameter of 2 mm., and react to light. There is a marked divergent strabismus. The veins of the fundus, examined after dilatation of the pupil with cocaine, seem considerably dilated. The supraorbital reflex is very active on both sides.

"The deep reflexes at the knee and ankle are considerably exaggerated and equally so on both sides. There is a prompt dorsal flexion of the great toe on each side in response to plantar stimulus. During the examination the patient has retched violently, but without vomiting.

"In the half-hour since admission the pulse rate has gradually dropped from 69 to 63 beats per minute, and the blood pressure has correspondingly and gradually risen from 160 to 185 mm. of Hg."

A lumbar puncture was subsequently performed, and 24 c.c. of bloody fluid under 23 cm. (water) tension was withdrawn, being a conclusive evidence of basal fracture with some intermeningeal hemorrhage and increase in intracranial tension.

As the accompanying chart (Fig. 1) shows, frequent observations on the pulse rate and arterial tension were taken during the day, and

inasmuch as there was no further increase in the latter beyond the 185 above recorded and considered a safe level, it was concluded that there was no indication for operative interference.

Symptoms, attributable largely to the effects of concussion, were present in this case—headache, nausea, dizziness on assuming an erect posture, etc.—all of which gradually subsided during the ten days following the accident, and *pari passu* with the return of the blood pressure and the pulse rate to their normal level (see Fig. 1). Doubtless the two conditions—concussion together with an increase of tension due to the intermeningeal hemorrhage—were combined, the latter showing itself as an early rise in blood pressure, the former as a late rise in

FIG. 1.

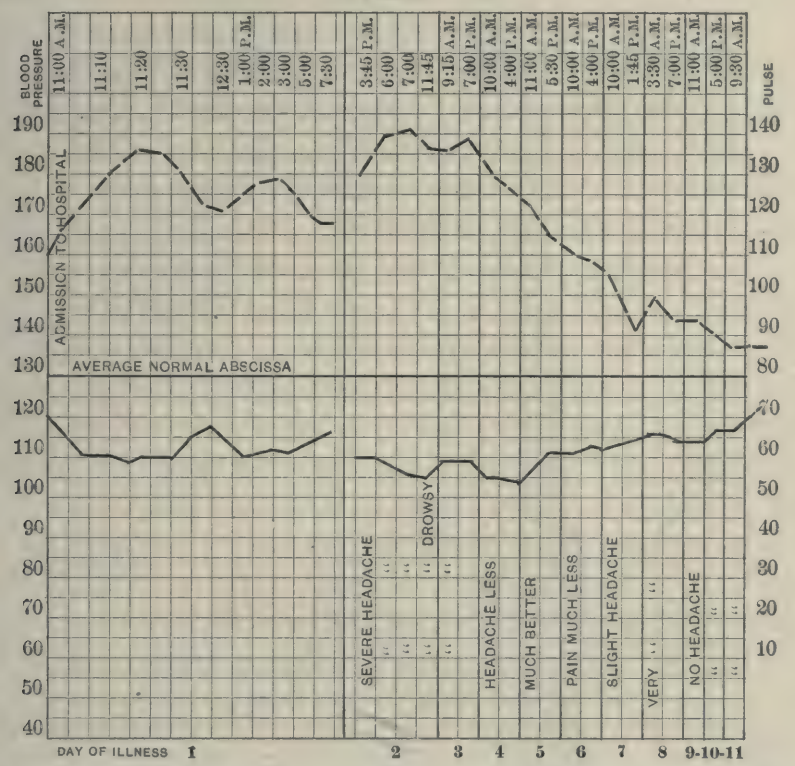


Chart of blood pressure (broken line) and pulse rate (solid line) in Case II. Note the increment in arterial tension and diminution of pulse rate on the day after admission, with gradual return to the normal during the ten succeeding days.

association with a certain degree of slowly-forming cerebral œdema, possibly of the type which Cannon[1] has ascribed to osmotic pressure, "which in brain tissue may attain a degree so much greater than blood pressure that the blood would readily be prevented from entering the cranium."

DISCUSSION. In this case the blow had been transmitted directly to the base of the cranium through the arch of the lower maxilla just as in the so-called "prize-fighter's fracture" of the skull—a form of injury not infrequently followed by a fatal outcome. The fracture

[1] Cerebral Pressure following Trauma. American Journal of Physiology, 1901, vol. vi. p. 91.

passed through the middle fossa and the temporal bone, and some degree of subdural hemorrhage ensued. A hemorrhage of this sort into the subdural space produces a condition which resembles as closely as do any other clinical ones the experimentally induced conditions of general compression—that is, conditions in which there is an equal distribution of increased tension throughout the entire cerebral chamber. The case is a representative one of a degree of cranial injury so frequently met in a traumatic service that it must be familiar to all. Under the circumstances no operation was performed, since it could have done nothing more than relieve intracranial tension, and there was no indication that this was necessary, since the process was arrested at a stage ("the beginning stage of manifest compression") in which there could have been no apprehension lest the vasomotor centre become fatigued in its regulation of blood pressure. Had the process advanced and given evidence of still greater tension, as shown by a further increase in the blood-pressure level, operative intervention might have become urgently demanded.

The effects of "compression" and those of "concussion" in a traumatic case are ordinarily distinguishable, in so far as the blood-pressure reaction is concerned, for in the latter case the rise, if one there be, will be tardy in its onset, in the former rapid. The occasion of the rise, however, is the same in both conditions, namely, an increase in the intracranial pressure, and it matters not whether this results from so-called "cerebral pressure" due to brain œdema, or to "cerebral compression" due to forces acting against the brain from without.

The beneficial effects of operations even in these border-line cases is often seen. On one occasion within the last year two young men, who had been thrown in a motor-paced bicycle race, were brought into the hospital at the same time. The injuries which they had sustained were practically corresponding ones, namely, a cranial fracture (compounded in one case) with some intermeningeal hemorrhage, as evidenced by lumbar puncture. Both patients were suffering from a pronounced degree of concussion. The low blood pressure registered in each case at the time of admission showed that there was no increase in intracranial tension. The compound case was operated upon by Dr. Follis, who elevated the fragments, and during the operation exposed the brain by an opening in the dura. The cerebral cortex was so ecchymotic as to present a cherry-red color, but gave no evidence whatever of an increase of tension. A piece of bone was permanently removed and the wound closed. This patient made a rapid recovery, showing none of the usual delayed post-traumatic signs of concussion, and after the first twenty-four hours was without subjective symptoms. The other, the unoperated case, remained in a more or less stuporous condition for several days, with headache, nausea, a rise in blood

pressure, and slowing of pulse, which gradually shaded off to the normal after a period of many days—a reaction which is frequently seen after cases of concussion (see Figs. 1 and 3).

Although far from advising operation in every border-line case of basal fracture with concussion, especially when blood-pressure observations show no great increase in intracranial tension, it nevertheless is evident from our records that, given two patients with supposedly similar lesions, the operated case with an opening left in the skull makes a more rapid recovery than the non-operated one, and, furthermore, seems to be less likely to suffer from the post-traumatic sequelæ of epilepsy and late mental derangements.

In the discussion of Case I. it has been noted that a local process even of considerable extent may call forth no symptoms characteristic of compression. If, however, such a process becomes more advanced so that its effects in upsetting the circulation are transmitted as far as the medulla, compression symptoms will be evoked. Unfortunately, for purposes of illustration, there is no case in my series in which a purely local process, as from an extradural hemorrhage, has inaugurated but not advanced beyond (as in Case III.) the early symptoms of medullary involvement. An analogous condition, however, is frequently seen during certain operative procedures which necessitate the elevation and compression of a lobe of the brain during extradural manipulations. Thus, the slowing of pulse and rise in blood pressure, which often accompanies the elevation of the temporal lobe in the Gasserian ganglion operation, has been emphasized heretofore and illustrative charts given.[1] The operative procedure on such an occasion becomes the equivalent of an experimentally induced compression carried to the "Anfangsstadium des manifesten Hirndruckes."

Case III. (Surgical No. 13,260.) *Simple linear fracture of the skull, vault and base, without concussion; extradural hemorrhage from rupture of A. meningea media; also, intermeningeal hemorrhage; severe compression symptoms; operation; recovery.*—The patient, a young man aged twenty-four years, a ship's carpenter by trade, was brought to the accident ward on April 17, 1902.

One hour before his admission, while directing the lodgement of a heavy piece of timber under the hull of a vessel, in some accidental fashion the beam slipped, and the patient's head was caught between it and the side of the boat, crushing the skull in "nut-cracker" fashion. He fell to the ground, bleeding from his nose and both ears. He did not immediately lose consciousness, as in cases of cerebral injury with concussion, but gathered himself together, stood up, and for some moments was able to ask and answer questions about the injury. During the course of the next half-hour he became gradually stuporous, and was brought to the hospital in an unconscious condition.

[1] Blood-pressure Changes in Surgical Cases, etc. Annals of Surgery, September, 1902.

The following note was dictated soon after his admission, 4.40 P.M.: "The patient is a well-developed young man. He is unconscious, and cannot be aroused by questions. He is restless and seemingly annoyed, reflexly, by slight peripheral stimuli, such as are occasioned by the taking of pulse and blood pressure, by the blood in his ears and nose, at which he is constantly picking. His pulse is 56 to the minute and of high tension. The respiration is 30 to the minute and regular. The blood pressure is high, measuring 230 mm. of Hg.

"*General Appearance.* The skin over the head, face, and neck is markedly cyanosed. Several veins over the forehead are prominent and of a deep-blue color. The eyelids seem swollen, as from congestion, and the network of venules over them is very evident. There is an apparent slight exophthalmos. The pupils are quite unequal, the right being almost pin-point in size, the left measuring 4 mm. in diameter. The axes of the globes are rarely quite parallel; at times, however, there is an equal conjugate deviation to the left.

"The only visible wound consists of a lesion of the right external ear, the pinna having been torn or rather crushed into two separate portions. There is marked tenderness on pressure over the temporal bone in the neighborhood of the ear, and there are beginning ecchymoses in this situation. Over the left parietal eminence the scalp is bruised and slightly swollen. There is considerable bleeding from the auditory meatus on both sides. Slight twitching of the muscles on the right side of the face is occasionally seen.

"The deep reflexes are possibly somewhat exaggerated with a suggestion of ankle clonus. No plantar response obtained. The temperature is 98.4°. The patient is not in a condition of shock."

An examination of the eye-grounds showed what was taken to be a marked dilatation of the veins.

During the hour subsequent to the making of this examination the patient's condition slowly but perceptibly changed for the worse. His stupor deepened, and he was much less easily aroused. The blood pressure rose steadily from 230 to 250 mm. of Hg., and the pulse meanwhile dropped, occasionally registering less than 50 beats per minute (compare chart, Fig. 2). The character of the respiration also changed for the worse. Distinct periodicities of a Cheyne-Stokes type became apparent, with no stage of complete apnœa, but with a period of quite shallow respiration, lasting about sixty seconds and alternating with a deep snoring stage of shorter duration. Associated with this rhythmic alteration in respiration, changes in other activities were distinguishable, such as a rise in blood pressure of several millimetres, and great restlessness, both corresponding with the snoring period of respiration, and at the same time the eyes were apt to swing over to the left. A condition of ptosis of the left eye also developed. It was considered inadvisable to delay a craniotomy longer. Up to this time there had been nothing to evidence any particular localization of trouble. However, during the handling necessary for the preparation of the scalp the tender area over the right temporal bone was pressed upon, so that the patient winced, and in doing so moved the left side of the face much more than the right. Until this observation was made it had seemed a matter of indifference upon which side the craniotomy should be performed, inasmuch as the symptoms were believed to be due solely to a general increase in intracranial ten-

sion, as in Case II., rather than to any localized collection of blood. The evident facial paresis might have been resultant to one of two causes: either an implication of the peripheral neurons of the right nerve in the fracture of the temporal bone, or to a left-sided anæmia of the cortex brought about by the local compression of an extradural clot in that situation. This uncertainty, however, was sufficient to favor the turning down of a flap from the left side of the brain.

FIG. 2.

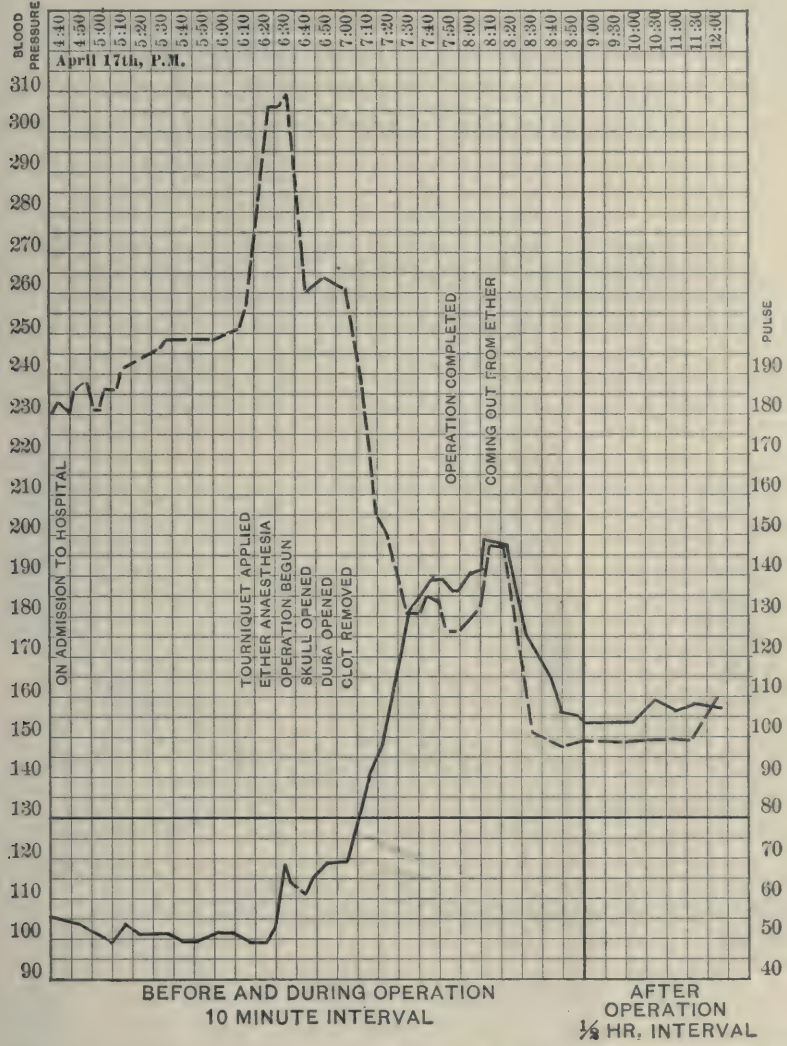


Chart of Case III. before, during, and immediately after operation. Broken line represents blood pressure in mm. of Hg. Solid line represents pulse rate.

That the surmise as to the probable location of the lesion causing this paralysis was a correct one, was shown by the fact that in the patient's struggles during the primary stage of anæsthesia there was evidence as well of considerable weakness in the right arm.

Operation, ether anæsthesia (one and a half hours after admission; two and one-half hours after reception of injury). As the blood-pressure chart shows, the application of the rubber tourniquet about the head and the administration of ether caused a great rise in arterial tension, namely, to 305 mm., almost an extreme level. It fell, however, nearly to its previous level before beginning the operation.

It is unnecessary here to go into full surgical details of the craniotomy. A large Wagner flap was turned down, its centre corresponding practically with the lower or facial portion of the cortical motor area. On elevating this flap a fissure was disclosed in the temporal bone crossing its entire extent, and passing down toward the base. Between the dura and the skull the upper edge of what was evidently a large blood clot was brought to view in the lower portion of the cerebral window. A further enlargement of the opening in a downward direction was necessary to satisfactorily expose it. This was rapidly done with Rongeur forceps, and a large clot, which had almost completely displaced the temporal lobe, was thus exposed. The clot was rapidly scooped out and the space it had occupied momentarily packed with gauze, as considerable fresh bleeding followed its removal.

FIG. 3.

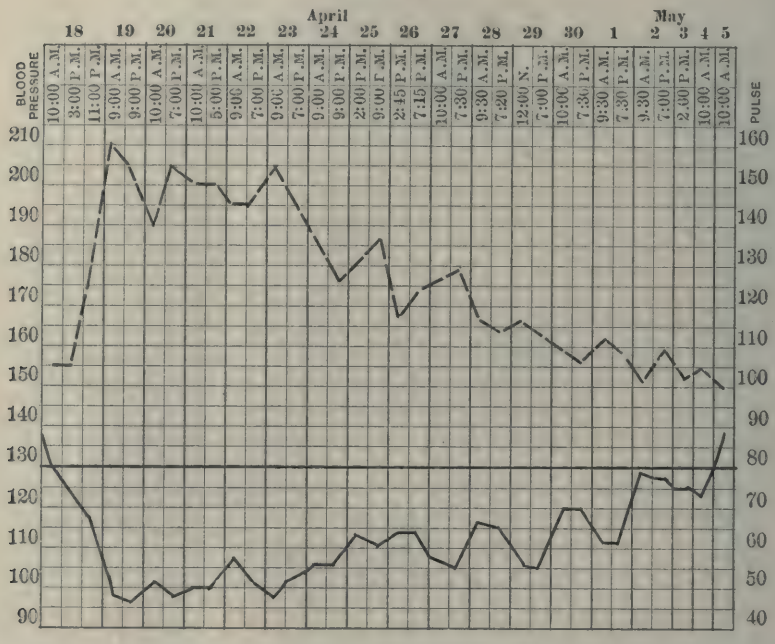


Chart of Case III. for the eighteen days after operation, showing post-operative evidence of secondary increase of intracranial tension, with gradual subsidence. Blood pressure, broken line; pulse rate, solid line.

The fissure through the bone could then be seen to run down across the base of the skull through the foramen spinosum, from which situation the bleeding was coming, probably from a ruptured middle meningeal artery.

The dura on first opening the skull was found to be very tense. It was opened, and an ounce of bloody cerebrospinal fluid under great tension was evacuated. It can be seen by consulting the blood-pressure chart (Fig. 2) that immediate relief was afforded to the extreme compression symptoms by the craniotomy and by the evacuation of the clot and superabundant subarachnoid fluid. The blood pressure returned to a safe level (150), and an accelerated pulse rate of from 130 to 140 momentarily took the place of the previous vagus pulse. Such an acceleration of the heart-beat is frequently seen in experimental conditions when there is a sudden release of the brain from

an increased tension which has previously produced vagus symptoms. The pulse soon slowed, however, and remained at 100.

The second chart (Fig. 3) shows the reaction during the period of convalescence and the gradual return to the normal of the increased blood pressure and slowed pulse, which on the day after the operation had once more shown a tendency to approach dangerous levels.

Discussion. I will not go into the details of the subsequent history of this case other than to say that the patient ultimately made a complete recovery. His condition cleared up very rapidly after the operation, although for some time he remained markedly aphasic. What is of interest for our present study, however, is the secondary rise in blood pressure and slowing of pulse shown in the chart (Fig. 3), which represents the average of the observations on pulse and blood pressure taken during the following two weeks. I can only explain this evidence of a secondary increase in intracranial tension, with its very gradual subsidence, by supposing, as in Case II. (Fig. 1), a condition of post-traumatic cerebral œdema of the Cannon-Bullard type. This relatively late reaction has been frequently seen in our traumatic brain cases.

The case is an unusual one from the rapid onset of the extreme symptoms of compression (Höhestadium des manifesten Hirndruckes). Here, again, was existent a combined process accounting for the increase in intracranial tension; on the one hand, an intermeningeal hemorrhage producing a certain general increase in intracranial tension much as in Case II., surmounted, on the other hand, by the local process consequent upon the extradural hemorrhage. This local process formed much more rapidly than is usual in case of extradural hemorrhage, probably owing to the fact that the meningeal artery was ruptured sufficiently low down to allow of a very rapid extravasation of blood. This hemorrhage in its upward progression, stripping away the dura from the skull, had finally reached and compressed the lower part of the motor cortex corresponding to facial movements at the time when the operation was commenced. Possibly either one of these two processes alone might not have sufficed to endanger the centres in the medulla. The two combined, however, produced a degree of compression which was rapidly approaching the "Lähmungsstadium" of the Germans. It is fortunate that relief could have been afforded so soon after the accident and before this stage set in. Operative intervention, when this third stage of compression is reached, is not always so gratifying in its results.

Examination of the Eye-grounds in States of Compression. It must be kept in mind that the underlying conditions which produce symptoms characterizing the various stages of compression are nothing more than degrees of interference with the normal intracranial circu-

lation, and that an increasing venous stasis is the first result of these circulatory disturbances. This, as has been pointed out elsewhere, may be readily appreciated during experimentally induced compression by the insertion in the skull of a close-fitting glass window through which alterations in the condition of vascularity of the exposed area of cortex may be observed, and in case the increase of tension is uniformly distributed ("general compression") these alterations may be taken as representative of the vascular conditions throughout the entire chamber. Fortunately, the ophthalmoscope offers a method of determining in clinical cases the presence or absence of intracranial venous stasis, inasmuch as the congestion is transmitted to and is easily observable in the veins of the fundus. Thus, the eye-grounds become almost equal in value to the experimental window. Unfortunately, however, during most of our operative procedures under anæsthesia the possibility of a continuous ophthalmoscopic examination is precluded, and although in several of our compression cases comparative examinations, before and after operative relief, have evidenced a diminution in the size of the veins in the eye-grounds this has never been seen at the exact time of its occurrence. An opportunity offered itself, however, on one occasion and under rather unusual circumstances which did allow an expert examination of the eye-grounds to be made at the very moment of giving relief to an advanced degree of intracranial tension. The patient on whom this examination was made was suffering from a pneumococcus posterior basic meningitis (Barlow), which had obstructed the foramina of the fourth ventricle and had led to an acute internal pyohydrocephalus. The increase of tension was such as to produce extreme symptoms of compression bordering on the terminal or paralytic stage. On several occasions the ventricles were tapped, and an ounce or two of seropurulent fluid evacuated with an immediate, though, unhappily, only a temporary amelioration of the symptoms, shown by a fall in blood pressure, an improvement in the pulse and respiration, and a considerable lessening of the mental stupor. These ventricular aspirations were easily performed without anæsthesia according to the method suggested by Albert Kocher for intraventricular injections, and during one of them Dr. Boardly followed closely with the ophthalmoscope the condition of the veins radiating toward the papilla. Immediately on removal of the ventricular fluid the veins, which had been tortuous and much engorged, became smaller in calibre, and lost much of their sinuous outline, while the arteries, on the other hand, became larger, more prominent, and seemingly more tortuous. Although I have frequently observed this change in dogs during the release of experimental compression, I am unaware that the observation has in so striking a fashion been made upon man. I think that too little stress is laid on the value of ophthalmoscopic examinations in the determination of

varying states of intracranial tension. Doubtless it is a difficult thing always to appreciate an increase in the size of the retinal veins, as they vary under normal conditions to such a considerable extent, but it should be possible with experience to recognize with some degree of probability the presence of this venous stasis, which plays such an important part even in the early stage of compression. It may be possible to gain this training by compressing the jugulars of patients on whom ophthalmoscopic examinations are being made. Dr. Boardly examined the writer's eye-grounds on one occasion while the inflatable band of a blood-pressure apparatus, which had been placed so as to encircle the neck, was gradually blown up. As soon as the recorded manometric pressure reached a level bordering on 80 mm. of Hg., an increase in size of the veins of the fundus became apparent. On a further increase of the pressure to 120 and 140 mm., or nearly to the level of arterial pressure, the veins increased in size fully one-third, and a sensation of dizziness, nausea, and stupor was experienced which quickly passed off on releasing the pressure. The venous stasis observable in the eye-grounds, of course, immediately disappeared.

CASE IV. (Surgical No. 14,081.) *Apoplexy with right hemiplegia; symptoms of pronounced intracranial tension evidenced by a blood pressure ranging about 300 mm. of Hg.; threatened symptoms of medullary paralysis; major symptoms (bulbar) immediately relieved by craniotomy and aspiration of intracerebral clot; Wagner flap left "ajar;" subsequent replacement of flap followed by return of symptoms; death on the third day from pulmonary complications.*—The patient, Frank W., colored, aged forty years, entered Dr. Halsted's service at 8 A.M. on November 23, 1902. On the evening of November 21st he was supposed to have fallen from a bicycle; was found in the street in a semiconscious condition, and was taken to the station-house as an inebriate.

At the time of his admission to the hospital, thirty-six hours after the onset of his symptoms, the following note was made on his condition:

"The patient lies in the dorsal position in a state of profound stupor, from which he can be aroused only in the slightest degree by the infliction of pain. There is an occasional aimless movement of the left arm or leg. The right side, with the exception of muscles supplied by the superior branch of the facial, is in a condition of complete paralytic flaccidity. His temperature registers 99.6°. The respiration varies in rate from 21 to 27. It is characterized by a distinct periodicity, a shallow and a stertorous, snoring period, alternating with considerable regularity. The pulse rate is regular, averaging 50 to the minute, and the arterial tension is very high. The blood pressure registers in the neighborhood of 300 mm. of Hg.

"Evidence of vasomotor rhythm is at times observable, the height of the blood-pressure wave corresponding with the period of deeper respirations, with restlessness and movements in the non-paralyzed side and with some pupillary dilatation.

"There is a persistent conjugate deviation of the eyes toward the right, associated with nystagmus. The pupils are equally contracted

and react to light. The veins of the forehead, median, and lateral are greatly distended.

"Reflexes: Deep reflexes readily obtained and are equal on both sides at the knee and ankle. They are not exaggerated. Superficial reflexes are abolished on the paralyzed side, plantar, cremasteric, and abdominal. They are present on the left. Visceral reflexes (sphincteric) are lost (?). McCarthy's reflex present on both sides.

"Anæsthesia, to painful stimuli at least, seems to be present on the paralyzed side. Some reflex response to pain can be obtained from the opposite side."

The history, such as could be obtained, indicated that the patient's stupor had been increasing, and in view of the great elevation in blood pressure and the beginning evidence of respiratory implication, it was determined to make an attempt to relieve the intracranial tension, and, if possible, to locate and evacuate the clot.

Operation, November 23d, 3 P.M. No anæsthesia required owing to deep stupor. A tourniquet was applied, and a large osteoplastic bone flap, measuring about 12 by 8 cm., was turned down from over the left hemisphere. Owing to the thickness of the negro's skull this performance, usually simple, was attended with some difficulty. The underlying dura was tense and without pulsation. On incising it, however, the brain bulged far into the opening, and began actively to pulsate. The convolutions were greatly flattened, deeply cyanosed, and the veins occupying the sulci were widely dilated and their contents so dark that the color contrast between veins and arteries was of an unusual degree.

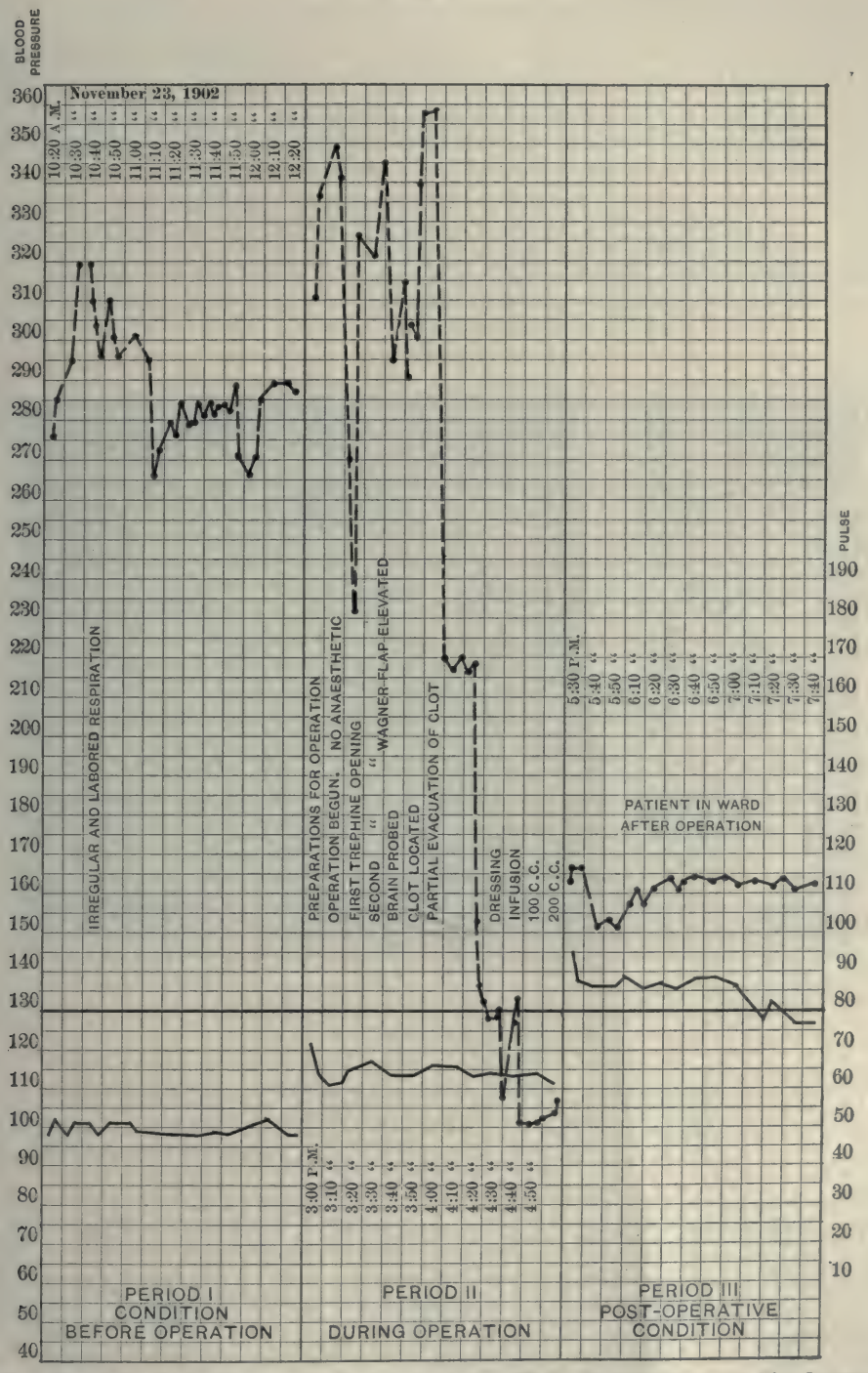
Through the convexity of one of the convolutions posterior to the fissure of Rolando a grooved director was passed into the substance of the brain in a slightly forward direction in the hope of tapping the site of hemorrhage. When the probe had entered a distance of 4 cm. a sudden lack of resistance was encountered as though it had entered a cavity, and dark, blackish fluid blood spurted out along the groove of the instrument. In the track of the director the handle of a scalpel, which was flat and had a sharp, rounded edge, was then introduced into the seat of hemorrhage. This was rewarded by the evacuation of about two teaspoonfuls of old, discolored, semifluid blood and clots. (A glance at the accompanying chart, Fig. 4, will show that the patient's blood pressure began abruptly to fall from its high level, approximately at 360 mm., and in the next twenty minutes had reached a normal level, there being, meanwhile, absolutely no change appreciable in pulse rate during this alteration in arterial tension, representing 230 mm. of Hg.)

The release from intracranial tension was evidenced by the immediate collapse of the bulging hemisphere. Two strips of rubber protective, to serve as drains, were passed into the cavity of the clot through the track which had been made. The bone flap was loosely replaced, no sutures whatever being taken in the skin. Strips of gauze were placed between the edges of the scalp and a loose gauze dressing over all. It was hoped in this way to allow for an elevation of the flap in safety-valve-like fashion, should there be once more a considerable increase in intracranial tension.

On November 24th, the day following the operative procedure, the patient's condition had greatly improved. The pulse rate and blood pressure remained within normal limits, his respiration was no longer

labored, his stupor was much less deep, and he could be aroused with considerable ease. He took nourishment by mouth for the first time since his "stroke," and at one time took a cup from the nurse's hand in order to drink himself. Slight voluntary movements of the right

FIG. 4.



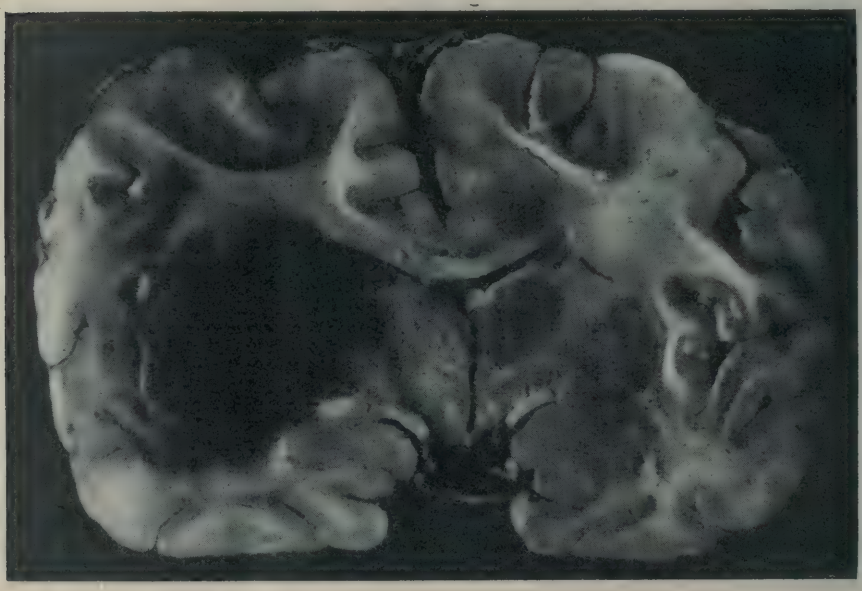
Broken line, arterial tension; solid line, pulse rate. Three fragments of the blood-pressure chart of Case IV. Note in Period I. the high tension and slow pulse. In Period II. the release from the vasomotor overaction by the craniotomy and evacuation of clot. Fall of blood pressure of 260 mm. of Hg. without change in pulse rate. In Period III. the practically normal levels after operation.

arm were also present. The conjugate deviation of the pupils had disappeared, and he seemed to see and recognize objects. He would endeavor to protrude his tongue on request. There was no effort at speech (note that the lesion extended far forward in the left corona radiata) at any time.

Owing to the great amelioration in the gravity of symptoms, it was thought probable that recovery would ensue, and at an ill-advised moment late in the afternoon of this date the dressing was removed, the drains withdrawn, the bone flap replaced, and the scalp sutured in place. A slight bulging of the brain was found at this time, and some compression was necessitated in readjusting the osteoplastic flap in position.

This misjudged procedure evidently turned the balance against the patient. His former stuporous condition during the following night again reappeared. Nourishment could no longer be taken, and respiratory difficulty again became evident.

FIG. 5.



One of the sections of the brain of Case IV., showing the situation and transverse extent of the cavity

When seen on the morning of November 25th the error of the previous day was apparent, and although the bone flap was once more elevated in the hope of readjustment, his condition gradually became worse. On the following day the lungs began to fill up, the right heart gave way, giving a definite regurgitant pulsation in the cervical veins, and at midnight of November 27th, three days and a half after the operation, death occurred. An autopsy was performed by Dr. Van Wart. The accompanying photograph (Fig. 5) of a section of the hardened brain shows the size and situation of the hemorrhagic cavity. It was found practically empty.

DISCUSSION. Considerable interest attaches itself to this case and to a previous case of apoplexy (surgical No. 13,892) from Dr. Osler's

wards, in which an attempt was made in a similar way to ward off a fatal outcome by the elevation of a large osteoplastic flap. In this earlier case the patient's condition was much worse, and the stage of respiratory paralysis, at the time of operation, was seemingly near at hand. The symptomatic relief, nevertheless, was striking, and the blood pressure fell immediately after opening the dura to an approximately normal level, at which it remained until death ensued from pulmonary complications, thirty-six hours later. The seat of hemorrhage in this earlier case, unfortunately, had not been sought for with sufficient freedom, and at autopsy a large clot the size of a hen's egg was found closely underlying the cortex and in exact correspondence with the opening in the skull. Had it been located and the cortex been freely incised the clot under great tension probably would have been forcibly extruded by the pressure of the surrounding brain.

The propriety of surgical procedures of this sort doubtless will be questioned by many, and I believe that only in exceptional cases will surgical measures hold out any prospect of success, and then only when the interpretations of blood-pressure observations are utilized as an indication for the necessity of intervention, as well as a means of estimating the degree of vascular relief gained by the trepanation. I am unaware that the attempt has heretofore been made with any rational intent to bring relief to the cases of extensive hemorrhage spreading from the capsule into the corona radiata, and I do not see any reason why we should exclude these cases from possibilities of surgical relief simply because the hemorrhage lies beneath the cortex, any more than that intracranial hemorrhage in other situations should be allowed to run its course. The majority of the cases of apoplexy which are exposed on the autopsy table show a large clot more or less readily accessible to operative attack, and one would be much chagrined to have an extradural hemorrhage of corresponding size brought to light post-mortem without an attempt having been made to remove it by operation. The underlying or major symptoms of compression are the same whether the collection of blood be extradural or within the substance of the brain itself. Whether the extravasated blood in apoplexy is in most instances rapidly coagulated or not can hardly be known until more cases have been explored before death, but it is presumable that it is and not improbable that the release of intracranial tension from the elevation of the bone flap, and especially from the evacuation of the clot, should one have been located, will, by the consequent rapid lowering of blood pressure, tend to check any further hemorrhage, even in case the ruptured artery should not previously have ceased to bleed.

The therapeutic measure generally advocated in case of intracranial hemorrhage with high-bounding pulse is a purely symptomatic one,

namely, "to bleed" the patient in order to lower blood pressure, the idea being that the persistent high tension is the cause rather than the result of the hemorrhage. If the interpretation of the experimental work is not at fault such an abstraction of blood with the idea of lowering arterial tension would be absolutely contraindicated, since the high blood pressure is only an indication of nature's effort to overcome the degree of intracranial pressure brought about by the foreign body in order to ward off an anæmic condition of the bulbar centres. Of course, the tension of the foreign body in this case, communicating as it does with a ruptured artery, is equal to that of the arterial tension, and were it not for its remoteness, ordinarily, from the medulla, death would almost immediately ensue, just as it does when a hemorrhage takes place in the near neighborhood of the medulla or reaches the fourth ventricle through rupture into one of the lateral ventricular cavities.

In the course of many of the experiments on compression the effects of blood-letting (the skull still being intact) were tried during the various stages of compression. At no time could any beneficial influences be seen, and if blood were withdrawn from the general circulation at a time when there had been a marked rise in general arterial tension to overcome cerebral anæmia, and in amounts sufficient to lower this vascular tension, the results were almost always disastrous unless a certain amount of reserve power remained in the vasomotor centre which could once more return the arterial tension to its former level. I would not mean to deny that symptomatic improvement ever follows blood-letting in cases of apoplexy in which the hemorrhages have not called forth pronounced symptoms referable to the vital bulbar centres, but when such is the case anything which tends to lower arterial tension without an associated opening in the skull to correspondingly lower intracranial tension is hazardous to say the least.

In dismissing these cases of apoplexy, representing as they do extreme types of the advanced stage of compression, it may be said that despite the ultimate failure of recovery in these two unfavorable cases, the temporary amelioration of the severe symptoms is a sufficient justification for future attempts to afford surgical relief to certain carefully selected cases of cerebral hemorrhage.[1]

CASE V. *Penetrating gunshot wound of skull; intracerebral hemorrhage; paralysis stage of compression with vasomotor and subsequent*

[1] Since writing the above note concerning the possibility of operative attack in apoplectic cases a patient has been in the hospital, under the care of Dr. Thomas and myself, in whom a subcortical hemorrhage had formed as the result of a stab wound of the cranial vault. A craniotomy was performed in this case; the clot was exposed, evacuated, and its cavity irrigated with salt solution; the bone flap was replaced, and the patient made a rapid and almost total recovery from the symptoms which the hemorrhage had caused. As in the case of apoplexy above recorded, the clot almost extruded itself through the opening made in the brain substance to reach it. Others have reported cases of recovery after operation for subcortical hemorrhages of traumatic origin.

respiratory failure; craniotomy during artificial respiration; long continuance of heart-beat; exitus.—The patient, a young woman, aged eighteen years, was brought to the hospital about 3 P.M. on April 21, 1902, soon after the reception of her injury. When seen in the accident room immediately after her admission it was recognized that she was almost in the "Lähmungsstadium" of compression, and rapid preparations were made for operation.

The only history obtainable was to the effect that she had been shot by her husband about one hour before admission. Examination showed that the bullet had penetrated the squamous portion of the right temporal bone, nearly 5 cm. above the zygomatic arch. Cerebral substance was protruding from and being squeezed through the wound; an invariable sequence of great increase in intracranial tension, when associated with a small opening through the skull and dura, which leaves the underlying brain unsupported. There was no wound of exit.

The patient was in deep coma. Her respirations were slow, gasping, and irregular, with periods of apnœa. The pulse was rapid, 160, of irregular rhythm, and the arterial tension was low. Blood-pressure observations, which were immediately instituted, demonstrated that a very rapid fall was taking place. The eyes were fixed, staring, and prominent, with widely and equally dilated pupils. The face was much cyanosed, and ecchymoses were already forming in the eyelids and conjunctivæ. She vomited soon after her admission, in projectile fashion.

It was apparent that she was advanced in pregnancy. Owing to the urgency of the case, further examination was not made, and the patient was hurried to the adjoining operating-room. On the way thither the respirations, which, in the few moments intervening since her entrance, had become much more irregular in character, ceased altogether. Artificial respiration, by thoracic compression, was kept up, until the patient could be put upon the table, when a rapid tracheotomy was performed, and a tube inserted in the trachea. After a moment of mouth-to-tube inflation, the color quickly returned to the deeply cyanosed face, and the pulse, which had continued during this interval, greatly improved in character.

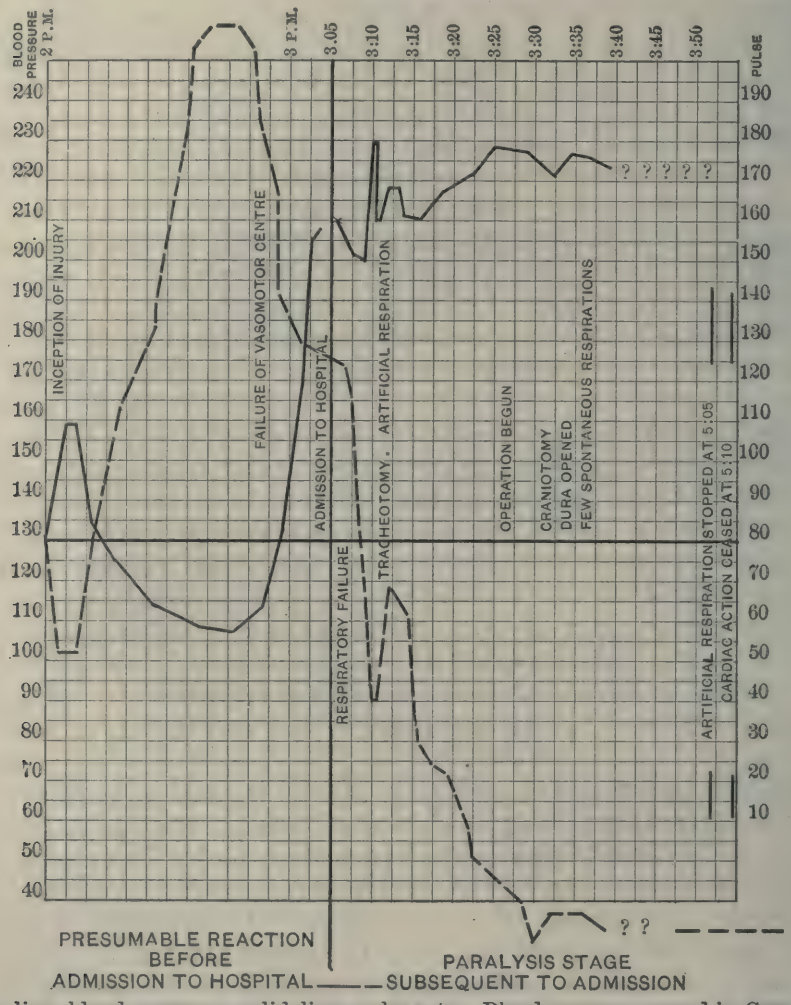
Meanwhile, an extensive area from the side of the scalp was being shaved; a tourniquet was applied, and a Wagner bone flap, the size of the palm of the hand, was quickly turned down.[1] There was a vain hope that the vasomotor and respiratory failure did not evidence an irrecoverable paralysis of the centres, and that prompt relief from anæmia, due to the extreme degree of intracranial tension, would allow of medullary circulation, sufficient to reawaken the centres to activity.

With three lives at stake—that of the assailant, his victim, and a child—the moments consumed during this partial hemicraniotomy under artificial respiration were exciting enough, and we were rewarded,

[1] In the absence of a motor with a burr and a Doyen saw a comparatively rapid way of making such a flap is to penetrate the skull with trephine or mallet and gouge in two places corresponding to the angles at the superior base line of the proposed flap. These openings may in a moment be rapidly connected with a Gigli saw and the two lateral edges cut out rapidly with the de Vilbiss forceps. Twelve minutes should suffice by this procedure for a safe exposure of a wide area of dura. A tourniquet should always be applied about the base of the cranium to control hemorrhage from the scalp during the procedure. This otherwise occasions much delay.

after the final opening of skull and dura, by the patient's taking, for the first time, a few spontaneous gasping inspirations. The hemisphere bulged under considerable tension from the opening, and a large amount of blood clot was evacuated. To our great disappointment, the voluntary efforts at respiration did not long continue, and it was once more necessary to resort to artificial means of continuing it. The blood pressure, meanwhile, had been steadily and rapidly falling (see chart, Fig. 6), until it had reached its level of complete vasomotor paralysis, representing only 20 to 30 mm. of Hg.—a condition from

FIG. 6.



Broken line, blood pressure; solid line, pulse rate. Blood-pressure record in Case V. Presumable reaction from the time of injury to death, two hours later. First portion of chart hypothetical.

which there is probably no recovery. The heart, however, like the isolated mammalian heart of the physiological experiment, continued to beat as long as its circulating blood was kept aërated by the continuance of artificial respiration. As long as there is cardiac pulsation, it is difficult to bring one's self to a realization of the actual presence of death, and artificial breathing was continued for two hours longer before its final abandonment.

Had the child been at or near full term, during the two hours and a

half of artificial respiration a Cæsarean section might, at any time, have saved it. During the craniotomy, however, the woman was examined by a member of the obstetrical staff, who pronounced the infant too premature to justify the procedure. On cessation of the artificial respiration, the patient became progressively more and more cyanosed, the heart-beat soon weakened, and, after two or three minutes, could no longer be auscultated.

Discussion. This case is cited not only as typifying the sequence of events in the so-called paralysis stage of compression, but also as an indication of what may be accomplished in rare instances under similar desperate circumstances. The accompanying chart (Fig. 6) records the observations which were actually taken after the patient's admission to the hospital, and also gives the reaction which by analogy with experimental conditions can be imagined to have taken place during the hour preceding, viz., a slowing of pulse and a great rise in blood pressure, which anticipated the failure of the vasomotor centre and resultant respiratory paralysis. Under just such circumstances in animal experimentation when intracranial tension has been increased so as to exceed the level to which arterial tension can be forced, or when the latter has been held at a high level long enough to bring about fatigue of the vasomotor centre, the life of the animal may be saved by the establishment of artificial respiration and a hurried release from the compressing force. It is impossible to say for how long a time a compression anæmia of the medulla in man may persist and still leave the respiratory and vasomotor centres in a recoverable condition. There can be no doubt, however, as evidenced by some cases which have been reported, that life may be prolonged by artificial respiration for a length of time at least sufficient to allow of operative relief from the compression. Every effort should be made after the craniotomy to restore once more the vasomotor tone, in case the simple release from pressure is not sufficient. Ordinary stimulants will not suffice for this, and it is to be hoped that when the therapeutic indications of adrenalin are finally laid down that it may prove to be the drug which can be depended upon to restore activity to cerebral centres which have suffered exhaustion from long-standing anæmia. In case hemorrhage is not under absolute control the administration of adrenalin is attended with risks, as the following incident will illustrate:

A patient was recently admitted to the hospital with a penetrating bullet wound of the brain, and very soon after admission, and while preparations were being made for operation, he passed into the "Lähmungsstadium" of compression, due to intracranial hemorrhage. Dr. Tinker performed a rapid craniotomy, which, as in the case reported above, did not suffice, through the release from pressure, to reawaken the activity of the vital centres. The blood pressure had fallen to its paralysis level, and artificial respiration had to be resorted to. Intra-

venous injections of a weak adrenalin-chloride solution were administered as a last resort, and, although the blood pressure could be held at any desired level during the infusion, the improved circulation did not suffice to restore activity in the paralyzed centres. The rise in blood pressure did nothing more than renew the bleeding from the wound in the bulging brain, and, on discontinuing the infusion, the pressure immediately fell to its pre-existing or even to a lower level. As in profound shock, so here, there seems to be an exhaustion of the vasomotor centre from overaction, which in the former state is brought about by reflex sensory stimulation, in the latter by direct stimulation of the centre from anæmia. The result in both instances is a profound and enduring drop in blood pressure, and, ordinarily, therapy is impotent to restore activity to the centre.

Isolated reports are to be found of procedures similar to that recorded above and carried out under artificial respiration in which there has been a successful re-establishment of voluntary respiration. These have been cases, I believe, almost without exception in which a cerebral abscess has been the cause of the increased tension and resultant medullary anæmia, and the prompt evacuation of pus has allowed a sufficient readjustment of circulatory conditions to reawaken the centres in the bulb.

Sir Victor Horsley[1] has called especial attention to the early respiratory failure under these circumstances, and has emphasized the fact that these cases "die from failure of respiration, and not, as is so often surmised, from failure of the heart."

The practical point which Horsley establishes in his communication is that there is a continuance of cardiac action after the respiratory failure, and consequently artificial respiration may suffice to prolong life in favorable cases until a craniotomy can be performed and the pressure relieved. In one of his cases respiratory failure, as in the case above reported, occurred on the operating-table; the skull was immediately opened, the brain bulged, the pressure was relieved, normal respiration was re-established, and the patient recovered.

It seems possible to retrace the sequence of paralyses of the centres one step farther than Horsley has gone, and to explain the supposed primary respiratory failure by a preceding vasomotor failure. Horsley and Spencer supposed that the medullary paralyses were produced by the mere mechanical effect of pressure exerted on the centres. Leonard Hill, however, in his classical monograph, gives experimental proof to show that it is rather the state of vascular anæmia which paralyzes the centres, and with this our experiments are in accord. Hill, however, does not mention the regulatory action of the vasomotor

[1] On the Mode of Death in Cerebral Compression, and its Prevention. Quarterly Medical Journal, July, 1894, vol. ii. p. 305.

centre which serves to ward off the condition of threatened anæmia by an elevation of blood pressure. The possibility of long continuance of cardiac action after primary vasomotor and secondary respiratory failure was shown by a case reported in the Mütter lecture,[1] in which under artificial respiration the heart-beat continued for twenty-three hours. Spencer[2] has recorded similar cases in which the heart-beat continued twenty-four, six, and eight and one-half hours after cessation of voluntary breathing. Macewen, likewise, in his well-known volume,[3] mentions other instances, in one of which breathing was re-established after some hours of artificial respiration. Hudson[4] has more recently added additional cases of the same sort.

To reiterate: After fatigue or failure of the vasomotor centre the blood pressure falls to a point below that of the intracranial or extravascular tension; anæmia consequently ensues; respiration, already embarrassed at this point, immediately ceases from total lack of vascularization of the centre, and unless relief is given the blood pressure gradually sinks to a level which represents irrecoverable paralysis of the centre governing it. Even when this has occurred artificial respiration with proper aëration of the blood may suffice to keep the individual's heart beating for hours.

In briefly summarizing the subjects of discussion in this paper, attention may be again drawn to the following points:

Varying degrees of rapid increase in intracranial tension produce corresponding disturbances in the intracranial circulation. To these circulatory disturbances the symptoms of compression are solely due. The condition known as acute cerebral compression may be conveniently subdivided into four stages, dependent upon the degree of circulatory alteration which has been reached. Each of the stages has its own more or less characteristic symptom-complex.

The major or underlying symptoms originate in the centres situated in the medulla, and are only called out when the degree of intracranial tension begins to approach the arterial tension so that anæmia is threatened. A circulatory condition in the medulla which borders upon anæmia has the effect of stimulating the vasomotor centre. Thus, a rise in blood pressure is occasioned which restores the local circulation. The extent of this rise may be taken as an indication of the degree of advancement of the compression. Beyond a certain point, however, this reaction cannot take place. The vasomotor centre

[1] The American Journal of the Medical Sciences, 1902, vol. cxxiv. p. 393.

[2] The Arris and Gale Lectures on the Central Nervous Mechanism of the Respiration. The Lancet, March 2, 1895, p. 533.

[3] Pyogenic Diseases of the Brain and Spinal Cord. Glasgow, 1893, p. 136.

[4] Respiratory Failure Occurring Before Circulatory Failure in Brain Injury and Disease. Medical News, June 10, 1899.

under these circumstances fails, and the respiratory efforts cease entirely.

In conjunction with other symptoms, a progressive increase in arterial pressure or a high degree of the same, which has been already reached, or a pressure which exhibits from moment to moment great alterations in level may be taken as a certain indication of the advisability of early operative intervention. In case there are localizable symptoms the site of trepanation is plainly indicated. In case of generalized compression from widespread hemorrhage when there are no localizing indications, the intracranial tension should be relieved by the elevation of a large osteoplastic flap from one hemisphere or the other with a corresponding opening in the dura.

A REVIEW OF SOME OF THE OLDER WRITINGS ON INFANT FEEDING.*

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It was my original intention to embody in this paper a review of the literature relating to maternal nursing, but this idea was abandoned when it was once realized how much there was to consider under substitute feeding. The gist of everything that has been written on maternal nursing can be summed up in a few words: All authorities in the past two centuries have advised mother's milk as preferable to all other forms of infant diet. Prior to this time, however, according to Van Swieten (Paul's translation, 1759), Van Helmont and his school opposed milk in any form.

Substitute Feeding. That much has been written on substitute feeding goes without saying. To do justice to all of it is obviously impossible. My comments, therefore, will be limited chiefly to the writings of the eighteenth century, which were at my disposal, and to the most interesting and important of the works of the first half of the past century, considering only a few of those which have appeared since that time. In doing this I will quote freely from those authors who have written interestingly and instructively.

The methods which have been in favor are three in number: (1) wet-nursing; (2) direct nursing from animals, and (3) the use of artificially prepared foods. All of the older writers are in accord in

* Read before the Section on Pediatrics of the New York Academy of Medicine, October 9, 1902.

preferring the first of these—*the wet-nurse*—although this measure has never been considered in any sense comparable to maternal feeding.

It has been impossible to fix upon the date of the beginning of wet-nursing as a common practice. It is probably safe to assume that it has been indulged in to some extent in all times. It has been a very prevalent custom in the times of which I write, and at certain periods was evidently practised to an extreme degree. John Clarke, writing in London in 1815, says that "The prevalent custom of relegating all children to wet-nursing or dry-nursing has resulted in reducing the supply of wet-nurses and in inducing the wet-nurse to forsake her own child, which invariably dies; therefore, it is hardly a question whether society at large is a gainer or loser by the employment of hired wet-nurses." The moral aspect of the wet-nurse question was evidently more commonly considered formerly than now. "This custom," Clarke goes on to say, "acts as a further detriment to society in that it leads to the neglect of older children, lack of attention to household duties, dissatisfaction with home surroundings, and consequent family differences." He thought that, "On the whole, it would be better perhaps that the children of the wealthy should be brought up artificially where the mother does not suckle them, because they would have every advantage of good nursing, cleanliness, air, and medical treatment, and would, therefore, have a better chance of living than the child of the wet-nurse." He suggested another plan to relieve the difficulty, namely, to have a vigorous wet-nurse feed both her own and the foster-child, the deficiency being made up artificially. John Roberton (London, 1807) refers to the same evils pointed out by Clarke, and suggests much the same remedies. He likewise considered it "the duty of the professional man to make the unfortunate infant deprived of its natural source of feeding every amends in his power."

Dewees (1825) preferred the sucking bottle to "the hireling nurse," unless it be known that the nurse is a person "capable in every respect of fulfilling the important duty of suckling." He pointed out that "the withdrawal of the wet-nurse from her own child and family, in benefiting one part of society, injured another." In order to obviate this, he suggested "that only those women who have lost their own children be employed." He was opposed to their nursing both their own and the foster-child, lest the latter receive too little nourishment.

The following rules laid down by Van Swieten as early as 1759 for the selection of a wet-nurse are most comprehensive and have not been much improved: "She should be examined by a physician, who should determine that she has perfect health; that her skin is natural in color, her eyes lively and animated, her gums firm and of good color, her teeth healthy and clean, her lips red, her habits of body neat and clean, and that no odor exhale from her mouth or nose or any other

part. He should also determine that her own child is well nourished." Beside "a prudent monthly nurse should examine every part of her body to exclude suspicious scars or pimples." "She should be from twenty-five to thirty years old, and it is best that she should have borne several children. Her breasts should be firm, distended, elastic, and of medium size." "Large breasts furnish little milk," and, according to Aetius, "in large breasts much swollen with the quantity of milk it becomes corrupted by remaining there, and consequently noxious to the child." "The nipple should be red, firm, and large, but not so large as to interfere with the freedom of the tongue's movements. The milk should run easily and spout a good distance like so many little siphons when the breast is pressed."

Rosen von Rosenstein (1776) indorsed the following lines from St. Marthe's *Pœdotrophia* (Tytler's translation) as covering all the points necessary to be considered in the selection of a wet-nurse:

"Choose one of middle age, nor old nor young,
Nor plump nor slim her make, but firm and strong.
Upon her cheek let health refulgent glow
In vivid colors that good humor show.
Long be her arms and broad her ample chest,
Her neck be finely turned and full her breast.
Let the twin hills be white as mountain snow,
Their swelling veins with circling juices flow,
Each in a well-projecting nipple end,
And milk in copious streams from these descend.
Remember too the whitish milk you meet
Of grateful flavor, pleasing taste and sweet
Is always best; and if it strongly scent
The air, some latent ill the vessels vent."

The securing of a satisfactory wet-nurse is not a purely modern difficulty. George Armstrong (1783) found that "a good wet-nurse is not always to be had, especially in or near great cities, where so many of them are given to drinking and other vices, and the worst of them will fall upon means of securing a good character." He found that the tendency on the part of the wealthy to indulge wet-nurses in all directions, especially in the giving of large salaries, "led to the ruination of many, making them as a class very unreliable." Clarke and many others refer to this, and several of the writers in the early part of the nineteenth century advised "that nurses owing to their loose morals be carefully guarded and deprived of all care of the infant, seeing it only at the time of nursing."

Direct Nursing from Animals. The second method of substitute feeding is one which has never come into common usage for several reasons: First, it has many repellent features; second, the milk of animals is not adapted to the digestive powers of infants; third, the method is not practicable. The goat, sheep, ass, and cow, the animals that have been in favor for this purpose, are not convenient household

pets, especially in our cities. Several of the earlier writers refer to the custom, and one or two practised it. Chambon (1799), for instance, preferred "suckling infants directly from a goat, a sheep, or an ass, to any form of substitute feeding." "The first," he found "very easy to manage, as goats proved susceptible to an attachment for the children which they nursed." He says "they come when full into the house and place themselves in a comfortable position to give the udder to the nursling."

At a much later period (1840) Andrew Combe quotes Dr. Von Ammon as advising that at the fifth month "the child should drain his food directly from the cow, and thus receive it in its natural state and at its natural temperature," and in support of his recommendation he says "infants fed in this way in the country thrive far better than those fed on cow's milk in towns."

Even at the present day in some parts of France infants are nursed directly from cows, and sometimes with good results. It is very probable that in Spain and Italy, where goats are commonly used as a source of milk supply, direct nursing is indulged in. Dr. Rotch (*Pediatrics*) refers to having observed a family of eight children "all of whom were nursed by the family cow, and were all healthy and strong."

It has usually been customary, however, when wet-nursing was impossible, to resort to some one of the various methods of artificial feeding.

Artificial Feeding. The foods which have been in most common use for this purpose are the milk of the ass, the goat, and the cow, broths made from the flesh of animals, and an innumerable variety of starch-containing and mucilaginous decoctions. The milk of the ass and the goat is still extensively used in some countries, and at one time was pretty generally preferred to that of the cow. It was early recognized, however, that the difficulty in securing the milk of these animals rendered this source of food impracticable. For this reason, the milk of the cow has been much more generally used. The milk of the ass and the goat, owing to its greater similarity to human milk, was usually given undiluted. The milk of the cow, on the other hand, has been given in a diluted form for many years. Judson and Gittings, in their recent work on *The Artificial Feeding of Infants* (Philadelphia, 1902), state that "the necessity of dilution to adapt cow's milk to the infant's powers of digestion was recognized as far back as the middle of the eighteenth century." They quote from the work of J. P. Frank, *On the Raising of Healthy Infants* (1749), to the effect that "Van Swieten, Loseke, and Cosner were the first to recommend diluted cow's milk for infant feeding; they advised to dilute from two to five times with water."

I have not had access to the writings of Loseke and Cosner to confirm Frank's observation respecting their methods, but in Paul's translation

of the *Aphorisms of Boerhaave*, with comments by Van Swieten, I find no reference to diluted cow's milk. It would not be surprising, however, to find that Van Swieten made some such recommendation, since his writings show evidence of an advanced and thoughtful mind. In some works of earlier date than this—the work of Walter Harris (1742) for instance—one fails to find any reference to the subject. Some of them do not even mention cow's milk, advising instead the milk of the ass or goat or some one of the various paps or panadas. Van Swieten quotes Von Helmont—who wrote in the very early part of the eighteenth century—as condemning the use of milk of all kinds, his objection being that "milk turns sour in the stomach." He preferred "a pap made with beer," which Van Swieten considered "a very singular preference which he did not satisfactorily explain."

The earliest reference I could find to the use of diluted cow's milk was in Sparrman's translation of Nicholas Rosen von Rosenstein's *Diseases of Children and Their Remedies*, published in 1776. He advised the use of "cow's or goat's milk—unboiled—diluted with water and sweetened with a little sugar." He sometimes used barley-water as a diluent, and where constipation existed he added a little thin filtered oatmeal gruel in which there had been dissolved a little clarified honey. He objected to the use of paps as "too gluey, tenacious and slimy and liable to produce obstructions in the mesentery, hardness of the stomach, acidities, wind, etc., by means of which we lose at least the one-half of our children." At the age of six months he gave whole milk containing rye biscuit which had been previously soaked in water. He fails to specify the amount of his dilution.

Underwood (1789) used somewhat similar but equally indefinite dilutions. He preferred either "water in which a piece of roll and some upper crust had been boiled, or hartshorn shavings boiled in water to the consistence that veal broth acquired when cold" as his diluent. To this mixture he added a little Lisbon or loaf-sugar. He, like Rosen von Rosenstein, was opposed to the use of paps and panadas in early infancy, but toward the end of the first year he gave some bread panada with broth.

George Armstrong, writing a few years earlier (1783), who considered himself well qualified to advise upon the subject of dry-nursing, in "that he had had some experience of it in his own family," directed as an adjuvant to maternal nursing "crumb of stale bread or, preferably, roll boiled in soft water to the consistency of pap, sweetened with a little soft or Lisbon sugar." For hand-fed infants, however, he directed that "cow's milk be added to their victuals as often as possible, and now and then some of it alone to drink." After weaning he used, in addition to other foods, "water in which the upper crust of bread had been boiled, mixed with an equal quantity of new

or boiled milk." This is the first instance in which the proportions of milk and water are indicated. It is probably safe to assume that the cow's milk used by this author as an adjuvant to maternal nursing, although not so stated, was a diluted milk. It is not probable that he would reserve the diluted milk for the latter months of the first year.

Moss (1794) gave much more definite directions for the modification of milk than did any of his predecessors. His ideas were advanced, instructive, and clearly expressed. He wrote thus: "Owing to trouble in the mother and inability to get a wet-nurse, it is sometimes necessary to secure some artificial food, for which purpose it will be advisable and proper to make choice of such food as appears to approach the nearest in quality to mother's milk. Ass's milk comes nearest to the human of any we are acquainted with, and, therefore, when it can be had it is very desirable and proper. Cow's milk being the only milk in general use, must be had recourse to, and will answer the purpose very well; but as it is a good bit thicker than breast milk, it will be necessary to reduce it to the proper consistence by diluting it with water. If the milk be good, about one part milk and two parts water will do very well to give at first. It is always best to err on the side of too great dilution." This mixture, which represents the same dilution as that advocated by the elder Meigs in 1850, was indirectly dependent upon some chemical analyses of cow's and human milk made by one Hoffman. This experimenter found that the inspissated residue obtained by the evaporation of cow's and human milk was as 13 to 8. On this basis Moss attempted the production of an artificial human milk by the dilution of cow's milk with water in the same proportion. This mixture seeming to the sight and taste so much stronger than human milk, he gradually increased the dilution until he obtained a mixture "possessing as nearly as possible the physical properties of human milk." His 1 in 3 mixture was the result; but even this, he says, "seemed a little less dilute than human milk." He did not consider the addition of sugar necessary unless the infant had been used to sweetened food. In preparing this food he used the freshest milk possible, preferring that just from the cow. He mixed at one time only enough to serve for a single feeding. This mixture he found could be advantageously substituted for mother's milk, and that "in general it agreed with infants much better than the other kinds of foods with which they were usually fed."

He was opposed to boiling, believing that this "made milk harder of digestion and binding; warming without boiling also did this, but to a less degree." In addition to milk he gave "chicken or veal tea to children who were dry-nursed," preferring the latter for the following very amusing reason: "It seems highly probable that the juices of

the young of those animals that feed upon milk are more likely to prove acceptable to the stomach of a child than those of the animals, as the cow, that may have formerly fed upon milk. The juices of the young sucking animals must be considered in a state approaching nearer to milk than those of other animals that do not derive their support from milk. Their juices, as partially abstracted by slight boiling, appear to be no other than milk somewhat more elaborated, assimilated, and animalized."

Struve (1801) used an equal quantity of milk and water in the preparation of a pap which he recommended. He considered the most wholesome beverage for children during dentition to be "equal parts of milk and water;" but when dry-nursing was first begun he advised "two-thirds of water to one of milk." "This should not be boiled, but heated to the boiling-point." He also highly recommended sweet whey prepared according to the following formula (Hufeland): "A slice of calf's stomach which had been prepared in vinegar and dried, should be soaked for two hours in a cup of water and then poured with the water into a pot of unboiled milk, from which the cream has been carefully separated. This is gradually heated, but not boiled. After a quarter of an hour the cheesy portion separates and the whey is left below. This should be poured off from the curds." He found that in the first months infants could live upon this alone.

Chambon (1799) used a mixture similar to that prescribed by Struve, but he preferred a preparation of grated crust of bread boiled in cream.

Heberden (1807) considered the object aimed at in artificial feeding to be the preparation of a mixture that resembles the mother's milk as nearly as possible. To accomplish this he used "ass's milk or milk and water with a little sugar of milk mixed with a little gruel, barley water, thin panada, or rice water, passed through a lawn sieve to insure their being smooth."

Roberton (1807), writing in the same year, found cow's milk objectionable at an early age on account of the large proportion of its curd; but cream diluted with five or six parts of water he used advantageously. He gave the preference, however, to "biscuit powder or small crackers boiled in water to a thin gruel, carefully beaten through a sieve and sweetened with fine sugar."

James Hamilton (1809) preferred "ass's milk or cow's milk mixed with a little water and sugar to which a small portion of milk biscuit may be added." He also used "arrowroot or patent sago mixed with water and milk, and to a less degree pap and panada." He added weak beef or chicken tea occasionally after the third month.

John Clarke, London (1815), whose work is very instructive and interesting, advised an "entirely fluid diet" that should be taken until the teeth appear. For this purpose he used ass's milk or "cow's milk pre-

viously skimmed, with two-thirds or three-fourths of its measure of gruel made from pearl barley, grits, rice, or arrowroot." "Where so mixed," he says, " the curd does not become so hard in the stomach as when diluted with water alone." As the child grew older the proportion of milk was gradually increased. Where this mixture disagreed he gave weak mutton, chicken, or beef broth, " clear and free from fat, mixed with an equal measure of any of the mucilaginous or farinaceous decoctions." After the appearance of the teeth he gave solid farinaceous substances boiled in water, beaten through a sieve and mixed with a small quantity of milk.

In instances in which the above preparations disagreed he sometimes obtained good results from a mixture of the farinaceous decoctions with a little cream.

Judson and Gittings, on the basis of this last suggestion, refer to Clarke as " one of the first to advocate the employment of cream diluted with starchy decoctions." As has been previously pointed out, Chambon, in 1799, recommended as useful a mixture composed of grated crust of bread dissolved in cream. His purpose in using this preparation—its " slight susceptibility to acid fermentation in the stomach" —was not the same as Clarke's. The latter added the starches for the same reason that they are often used to-day, namely, to break up the thicker curd of cow's milk. When so mixed, he says " the curd does not become as hard in the stomach as when diluted in water alone." So while their practices were much the same, and their results probably akin, the principles on which these results were based were entirely apart.

Dewees (1825), whose work seems to have been closely followed by other writers for many years, advised a mixture composed of milk two-thirds, water one-third, and " a small quantity of loaf-sugar." He used pure home milk as fresh as possible and from one cow. He gave very explicit directions regarding the preparation and care of his milk mixture. He advised that each feeding be prepared separately, that it be heated by the addition of hot water or on the sand-bath, and that the milk be kept in a cool place, and when in the least acid, rejected. Milk should never be boiled. In hot weather " it is true the tendency to decomposition is diminished by boiling; but this can be as satisfactorily accomplished by putting it, closely covered, over a hot fire and bringing it to the boiling-point; so soon as this is reached it should be removed and cooled as speedily as possible." " This plan prevents in a great degree the formation of the strong pellicle on the top, which deprives the milk of a portion of one of its most valuable parts."

James Kennedy (Glasgow, 1825), writing in Scotland in the same year, advocated what is, as far as I can ascertain, the first cream and whey mixture. He says " such forms of prepared aliment are preferable,

as they consist of milky and farinaceous substances agreeably sweetened. Of all these, recent cream of cow's milk diluted with whey (made from rennet) and arrowroot appear, from experience, to be the most congenial." He did not specify the proportions of the different ingredients used.

During the fourth decade of the nineteenth century little new was added to the methods of infant feeding. Practically all of the writers, as has been intimated, adopted the recommendations of Dewees. Marshall Hall (1831) preferred "pure beef tea without spice and with or without sago" to any of the milk foods. Eberle (1833) advised "farinaceous decoctions mixed with a small portion of cream" where no other form of milk could be given, and Combe (1840) advocated "fresh cow's milk, tepid and diluted with half or more of water and slightly sweetened." Cow's milk given in this way he considered "decidedly preferable to gruel, panada, arrowroot, chicken tea, or any other preparation less analogous to the natural food of the child." When children were artificially fed from birth the first food he suggested was composed of "two-thirds of pure fresh water added to one-third cow's milk. Goat's or ass's milk does not require more than an equal quantity of water." "After a week or two the water may be reduced to one-half, and later to one-third, at which proportion it should be continued for four or five months." This dilution, it is noted, is greater than that recommended by Dewees and his successors, and the attempt is here made to gradually increase the strength of the mixture as the age advances. Combe urged the utmost cleanliness regarding the care of dairy implements, and considered the excellence of dairy products in "Holland and other places" as "due almost entirely to this single cause."

It was not until the elder Meigs, in the second edition of his work on *The Diseases of Children* (1853), published his revolutionizing formula that the subject of infant feeding received a new and much-needed impetus.

Meigs was the first writer to appreciate the necessity of adding cream in order to obtain a proper fat percentage in his mixture. The mixture known for so many years by his name was prepared as follows: "A scruple of gelatin was soaked for a short time in eight tablespoonfuls of cold water and then boiled until it was dissolved, for about ten or fifteen minutes. To this was added, with constant strirring and just at the termination of the boiling, one-half pint of milk and arrowroot, the latter being previously mixed into a paste with a little cold water. After the addition of the milk or arrowroot and just before the removal from the fire, eight tablespoonfuls of cream were poured in and a moderate quantity of loaf-sugar added." The proportions of milk, cream, and arrowroot were made to depend upon the age and digestive

powers of the infant. For a healthy infant of a month he gave from three to four ounces of milk, one-half to one ounce of cream and a teaspoonful of arrowroot, to one-half pint of water. For older children the quantity of milk and cream was gradually increased to one-half or two-thirds milk and from one to two ounces of cream; the gelatin and arrowroot remaining the same.

Judson and Gittings state that in the seventies Meigs advised a mixture of equal parts of milk, cream, lime water, and arrowroot water, sweetened with a little sugar. This formula, which they mark as "the fountain-head" of all the later advances in milk modification, is not mentioned in any of the several editions of his work, and must have been obtained from some other source. It would really seem more fitting to mark the earliest formula of Meigs as "the fountain-head," since it was success in the use of this formula that led to the preparation of a monograph entitled *Food for Babies*, by William Henry Cumming, M.D., of Williamstown, Mass., and published in New York in 1859. In the preface to his work he eulogizes the writings of the elder Meigs, and points out that it was the success he met with in the use of the Meigs formula that stimulated him to a careful study of the subject of infant feeding, the result of which he so well presents in the work under discussion. This author approaches more nearly to a scientific modification of cow's milk than anyone who wrote prior to his time or for many years after. He says: "The milk that is adapted to a newborn calf is not suitable to an infant. It must be modified, or else it will do harm rather than good. Everyone knows that an infant cannot bear pure cow's milk, and everyone adds more or less water to weaken it. There is too much casein in cow's milk, and the infant cannot digest it. There is almost three times as much as in human milk, as seen by the following tables:

"In 1000 parts of cow's milk there are of	Butter	38.59 parts.
	Casein	40.75 "
	Sugar	53.97 "
	Water	866.69 "
"In 1000 parts of human milk there are of	Butter	20.76 parts.
	Casein	14.34 "
	Sugar	75.02 "
	Water	889.88 "

"Therefore, to reduce the casein of cow's milk to the proportion found in human milk, we must add one and four-fifth times, or nearly twice, as much water. Milk thus diluted will not be likely to disagree with the child's digestion; but after a time one will find that the child is not thriving on this diet, for the reason that the proportion of butter has been diminished with that of the casein from 38.59 to 13.58—just about two-thirds of the proportion existing in human milk (20.76)—a proportion which is far less than the infant demands.

"To those at all familiar with the elements of arithmetic it will be evident from comparing the relative proportions of the ingredients that dilution of ordinary cow's milk will never enable us to imitate the composition of human milk. It is possible, however, to obtain a milk having this composition in two ways: First, by taking the upper third of cow's milk that has stood for four or five hours, which has the following composition: butter, 54; casein, 38; sugar, 52; water, 856. By adding to this sugar 142, and water 1458, and dividing by 2.6 to reduce it to thousandths, we obtain a mixture having practically the composition of human milk. Another and in warm weather a better way is by taking milk from the latter half of that given by the cow. The first part contains very little butter, the last part is very rich—about 56 parts in 1000 in butter. This milk when diluted with one and one-half parts of water and properly sweetened resembles ordinary human milk."

That he appreciated the necessity of varying dilutions for varying ages is evident from what follows: "Mother's milk for the first two weeks after birth has a peculiar composition. From its first appearance it gradually changes until it becomes ordinary milk. Our mode of feeding involves the imitation of these several qualities of the milk. We call our substitute 'artificial human milk.'" The method of obtaining a milk to meet these various requirements is indicated in the following table, which shows the quantities of milk, sugar of milk, and water required for the various age periods. His formulæ are expressed in the proportions of the different ingredients contained in 1000 parts of milk. Thus 1000 parts of the milk taken from the upper third of cow's milk which has stood for four or five hours, as previously stated, contains 54 parts of fat, 38 of proteids, 52 of sugar, and 856 of water.

In order to obtain the proper proportions of the ingredients for the different age periods, he adds to this top milk, which is especially rich in fats, certain amounts of water and milk sugar. Being curious to know exactly what this table represented I have worked it out, and in so doing obtained some very interesting results.

He prescribed a mixture of the following strength:

	F.	P.	S.
For the age of 1 month	1.5	1.1	7.4
" " 2 months	1.8	1.3	7.4
" " 3 "	2.0	1.4	7.4
" " 4 "	2.3	1.6	7.4
" " 5 "	2.6	1.8	7.4
" " 6 "	2.7	1.9	7.4
" " 7 " and 8 months	2.9	2.0	7.4
" " 9 " to 10 "	3.0	2.1	7.4
" " 11 " to 13 "	3.1	2.2	7.4
" " 14 " to 17 "	3.3	2.4	7.4
" " 18 "	3.5	2.4	7.4

For children under one month he made his mixtures by diluting the upper eighth of a bottle which had stood for four or five hours, making his dilutions much greater.

It is to be assumed, since Cumming does not state that the analyses which he used are borrowed from others, and since they do not quite agree with any of those made prior to his time, that he made his own. In so doing he has been in error in considering the top milk he used—the upper third of milk which has stood for four or five hours—to contain but 5 per cent. of fat. According to Chapin's table, this milk should contain about 10 per cent. of fat, which would, of course, practically double the fat percentages indicated in his table. Had he restricted himself in the preparation of his mixtures to the milk obtained in the latter half of the milking, assuming as he does that this was a 5 per cent. milk, he would probably have more nearly obtained the results he thought he had obtained by the other method.

Cumming fully recognized the limitations of these formulæ. Thus he says "this schedule is arranged to suit the wants of vigorous children, but in using it great care and skill are needed. Regard must be had not to the mere age, but to the condition of the child. One child goes on prosperously to the age of six months; he is in every sense six months old. The dilution directed for that age will suit him exactly. Another during his third or fourth month is sick and feeble. On learning these facts and observing his condition we should say: this child was born, it is true, six months ago, but his time has been ill spent; he has not made the usual progress; we must reckon him as only four or five months old. To such an one we give the milk suited to the seeming age. It is indeed always safer to begin with milk somewhat more diluted than the child's age indicates and to increase its strength as the case will permit. It is less hurtful that the food should be insufficient than that it should be indigestible. . . . If a child using this milk becomes sick it is well to diminish at once the strength of his food to that of a child three or four or sometimes (in severe cases) six months younger."

He also appreciated the value of increasing the percentage of fat where there existed a tendency to constipation; thus he says: "It will sometimes happen that, while using milk prepared according to the foregoing directions, constipation may occur. An addition of butter to the milk will here be useful." He follows this by an explanation of the manner in which the fat percentages may be increased.

He evidently met with the same obstacle in applying this plan of feeding that often confronts us in our attempts to feed infants from the laboratory, namely, the cost. He says "this prepared method of artificial lactation involves much care and expense. The excellence of our plan is not that it costs nothing, but that it will repay the parent

for all the labor and money expended. How much money is yearly expended in securing medical aid for children who need not medicine but food?"

These quotations from this very interesting work are sufficient to make it evident that a successful effort at definite percentage feeding was made at an earlier period than we have hitherto thought. It is difficult to determine how extensively this booklet has been read, but since one finds no reference to it in the text-books on pediatrics, it is probable that this careful, observing, and original author made a valuable contribution to the elucidation of an obscure subject without even obtaining an audience for his opinions.

The development of percentage feeding beyond this point, including the works of the younger Meigs, of Rotch, and others, is so familiar to all of us that it is unnecessary to consider it in this communication.

It is sufficient to say of the *starchy* and *mucilaginous preparations* and the various *animal broths* and *teas*, that they have been prominent constituents of the infant's dietary in the period covered by the literature which has been reviewed and probably for many years prior to that time. Many of the older writers preferred them to milk in any form, while the majority of those who preferred milk permitted the use of these substances as additional foods. Still another class prepared their paps, panadas, etc., with milk instead of water, thus combining the two methods.

The so-called pap or panada—the terms are sometimes used synonymously and sometimes to describe different preparations—have been very variable in composition. Des Essartz (1760) gave the following directions for pap: "Put in a copper or iron kettle (preferably the latter) some fine wheat flour. Cover this with cold cow's milk added little by little. When thoroughly mixed cook until thick." The degree of thickness should vary with the age of the infant.

Armstrong (1783), on the other hand, used "the crumb of stale bread, roll, or biscuit boiled in soft water to a proper consistency sweetened to taste like new milk." This latter method probably conforms more nearly to that adopted by the generality of writers.

Broths have been almost universally sanctioned as a part of the diet of the latter months of the first year. Only one writer—Marshall Hall—seems to have placed them before all other food preparations.

Before bringing this essay to a close, it seems desirable to consider the implements which have been used in the administration of artificial foods. They are the boat, the spoon, the sucking horn or bottle, and the pot of Dr. Hugh Smith. But one reference is made to the last mentioned, and that is by Underwood (1789). "It is formed," he says, "in the shape of an Argyle or gravy pot, with a long spout rising from the bottom and pierced only with a few small holes at the end, which

is to be covered with a piece of vellum or parchment which, being left loose a little way over the spout, is as soft and pleasant to many infants as the breast. The boat, spoon, and horn are in no way comparable to it." He advised strict cleanliness in its use.

The spoon is referred to but not recommended by Des Essartz (1760). He graphically describes and bitterly denounces the filthy methods resorted to by nurses in the use of this instrument. He says: "After putting the pap in the spoon they carry it to their mouths, cool it off, return it to the spoon and then give it to the infant." "Some nurses, not wishing to use the spoon, place their index fingers in the food, which after cooling, they permit the infant to suck."

I have endeavored to fix upon the date of introduction of the nursing horn or nipple, but without success. Among the writers I have consulted, Rosen von Rosenstein (1776) was the first to recommend the sucking horn. From his reference to it, one would infer that it had not been much used outside of Russia prior to that time. He writes thus: "If we cannot procure a nurse and the mother cannot suckle her child, then we must accustom the infant to suck by means of a little instrument called a sucking bottle, which is universally used in eastern Bothnia with great advantage; but this machine ought always to be kept clean. It is to be made of a horn, the smaller end of which may be fastened to a tanned skin of a cow's teat, or if this is not to be procured we may use any other thin skin pierced with many small holes."

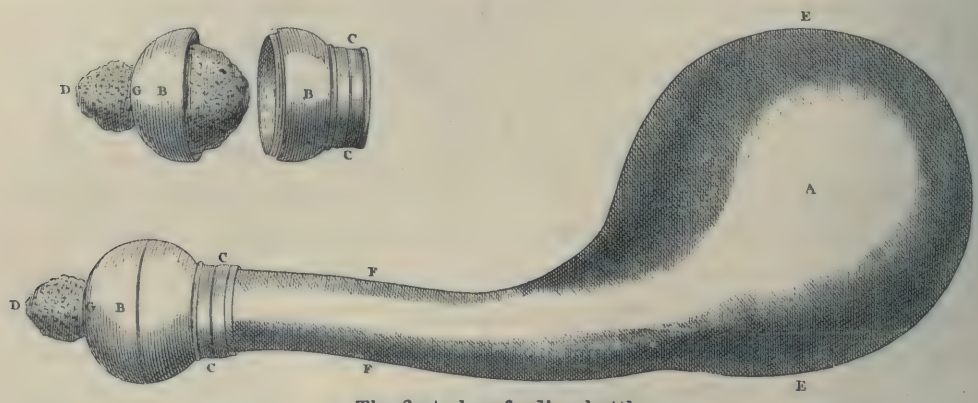
Armstrong (1783) describes this instrument in the following manner: "The horn made use of for suckling is a small polished cow's horn which will hold about a gill and a half; the small end is perforated and has a notch around it to which are fastened two small bits of parchment, shaped like the tip of a finger of a glove and sewed together in such a manner that the food poured into the horn can be sucked through between the stitches." This description marks a slight improvement in the manner of preparation of the horn and suggests a new substance for the artificial nipple.

In 1794 Moss described "a machine made of horn or *tin* so contrived that the child sucked his food from it as from a breast."

In 1786 Baldini described what was probably the first glass nursing bottle, a sketch of which is submitted for inspection. (See illustration.) He says of it: "This bottle, made of glass or crystal, is surmounted by a hollow metal knob which is gilded so that it will neither rust nor collect verdigris. This knob is divided in its centre into equal portions which screw together. The distal portion is perforated by a small aperture, through which a portion of a sponge placed in the hollow part protrudes. The protruding portion of the sponge represents the portion from which the child sucks."

For the poorer classes he advised "an ordinary bottle capped with

a piece of chamois." The chamois was "open at the end and surrounded a piece of sponge which extended into the neck of the bottle and protruded through the opening described. He advised that this apparatus "be washed many times each day in tepid water."



The first glass feeding bottle.

Chambon (1799) recommended a feeding bottle, evidently referring to a glass bottle, "the orifice of which was closed with a linen rag or piece of sponge to prevent the milk from running too rapidly." He says, "I will not describe the methods which have been published to simulate the breast nipple," from which one would infer that there had been many. He, like his predecessors, insists upon scrupulous cleanliness in the care of this instrument, "as otherwise it contracts a disagreeable taste, disgusts the children, occasions vomiting, and infects the milk, causing it to change rapidly in the stomach."

After this date both the horn and bottle were recommended, the horn rather more than the bottle, until Dewees, in 1825, recommended "a flat oblong nursing bottle covered with a properly prepared cow's teat." He insists that "much care be given to preserving it sweet. One should never put a second supply of milk or food upon the remains of a former. The bottle should be emptied after each nursing and immediately cleaned with hot water; it should then be thrown into and kept in a basin of cold water in which there is a little soda dissolved, and, before being used, well rinsed with clean cold water."

He prefers the heifer's teat to any other form of nipple, and urgently recommends that it be prepared "by those who understand this art." It must not be too large or permit too rapid a flow of the food. It should always have a piece of sponge in it to control the flow. Both the teat and the sponge should be well washed after each feeding and be kept in whiskey and water. Clean thread should be used each time the teat is tied on." He also refers to a tube which was in use at this time, and condemns it, owing to the difficulty of keeping it clean.

In 1833 Dendy recommended as a nipple "washed leather or the teat of a young heifer, in which a small piece of sponge is placed in

imitation of the pores of the nipple, to prevent too rapid a flow of milk. The first is more easily kept clean, but the latter more acceptable to the infant; indeed, more eligible, as it brings the necessity of constant cleaning." He advised keeping it between feedings in rose or distilled water to which a few drops of spirit of wine had been added.

Combe (1840) advised either washed leather, chamois, or a few folds of fine, soft linen, pierced with a small hole for the mouth of the bottle. "Sometimes a small piece of sponge covered with a rag, or the *artificial cork nipple recommended by Dr. Bull*, may be preferred. Whatever material is used, great care must be taken not to have the holes too large." This author quotes Erdman as saying that "the peasantry in Russia, even at this late date, are using, instead of a nursing bottle, a cow's horn with a small hole at the point, over which a cow's teat is tied. The teat is placed in the child's mouth, the milk poured in at the larger end of the horn and the child left to suck at pleasure." And Van Ammon says that "among these people the horn is not cleaned and frequently the teat passes into a state of putrefaction."

Churchill (1850) used chamois or cow's teat for a nipple, preferring the latter, and also described a thin elastic cork nipple invented by M. Dardo, of Paris, and *one of ivory* from which the earthy matter had been removed and which was flexible and elastic. He did not consider them as satisfactory as the calf's teat, "being far too short."

The first reference I have been able to find to a rubber nipple appears in the work of Tanner, published in Philadelphia (1861). He advises a nipple formed of *vulcanized India rubber*. S. Barker (London, 1864) recommended a nipple made of ivory, cork, *India rubber* or wash leather.

The high mortality in earlier times among the artificially fed (six in eight, according to Dr. Merriman, quoted by Dendy), in the light of what has gone before, would seem to have been not so much dependent upon defective formulæ as upon the poor methods of administration and probable lack of care in collecting and preserving the milk.

NOTE.—Since writing the above I have discovered that the first communication of William Henry Cumming, M.D., on the subject of diet in early life appeared in THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES for July, 1858, N. S., vol. xxxvi., p. 25, under the title, "On Natural and Artificial Lactation." This article formed the basis of his monograph. It demonstrates clearly that the chemical analyses quoted from the monograph were the results of his own work.

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A CASE OF GANGRENE OF THE LUNG CURED BY OPERATION.*

By David Riesman, M.D., A. C. Wood, M.D.,

AND

G. E. Pfahler, M.D.,

OF PHILADELPHIA.

The history of the case is as follows:

I. P., a negro, aged sixty-three years, born in Delaware, was admitted to my wards in the Philadelphia Hospital on July 22, 1902. His mental condition was such that a complete history was not obtainable, but it was ascertained that his family history was good and that his own health had always been satisfactory.

* Read before the College of Physicians of Philadelphia, December 3, 1902.

The illness, on account of which he entered the hospital, began four days prior to admission, with chill, pain in the right side, and cough. Examination showed the patient to be an emaciated man, with excessively tortuous temporal arteries, and hard, beaded radials, with arcus senilis and contracted pupils. His skin was hot and dry, the tongue coated, the breath offensive, the temperature 103.6°, the pulse 110, hard and incompressible, the respirations 36. The chest showed diminished expansion on the right side. The percussion resonance was impaired over the middle of the right lung posteriorly, and in the middle of the right axillary region. Over this dull area fremitus was increased. Auscultation did not afford any satisfactory revelations. The heart sounds were feeble, except for the second aortic, which was accentuated.

The temperature remained elevated—between 102° and 103.4°—for two days. During the night of July 24th it fell rapidly from 103° to 98°, without any sweat. The respirations dropped to 28, the pulse to 88. Within a few hours, however—by 11 A.M.—the temperature had again risen to 101.6°, declining by the following morning at eight to 97.8°.

Examination at this time revealed very little of moment in the chest. No distinct area of consolidation could be discovered, and, judged by the physical signs, the man's condition had greatly improved. The symptoms, however, did not show a corresponding amelioration. Despite the fall in temperature, pulse, and respiration rate, the patient's state appeared grave. He was delirious and struggled to leave the bed, had insomnia, coughed a great deal, and passed urine and feces involuntarily. During the time in which the quantity of urine was measurable, it was from twenty-two to thirty ounces; it contained albumin and an abundance of hyaline and granular casts, was acid in reaction, and had a specific gravity of 1020. The bowels were loose, greenish in color, and very offensive. There was no enlargement of the liver or spleen.

The temperature remained decidedly subnormal for four days, between 96° and 98°, the highest point in the day being reached at either 8 P.M. or 2 A.M. Only once during the four days did it ascend above 99°. The breath was offensive, especially during coughing, and on July 28th the resident physician, Dr. Dalby, noticed that the sputum had a gangrenous odor. In a specimen examined at this time I was not able to find elastic tissue or fatty acid crystals. Tubercle bacilli were also absent.

An examination of the chest made on July 28th showed the following: Slight impairment of resonance on the left side, in the first and second interspaces in front; a normal note elsewhere over the left chest. On auscultation the breath sounds were found to be feeble over the entire left side, including the area of slight dulness. Here, however, the expiration was a trifle prolonged, but neither harsh nor bronchial. On the right side nothing was found in front; posteriorly, however, important physical signs were discovered. There was a dull patch to the inner side of the lower half of the scapula, in the scapulovertebral space, the dulness extending downward and forward to just behind the postaxillary line. Over the dull area, especially in the spinal gutter, tactile and vocal fremitus were increased. On auscultation bronchial breathing could be heard over a small area inside of the

lower half of the scapula, close to the spine, at the level of the fifth rib. Below the angle of the scapula the breath sounds were normal,

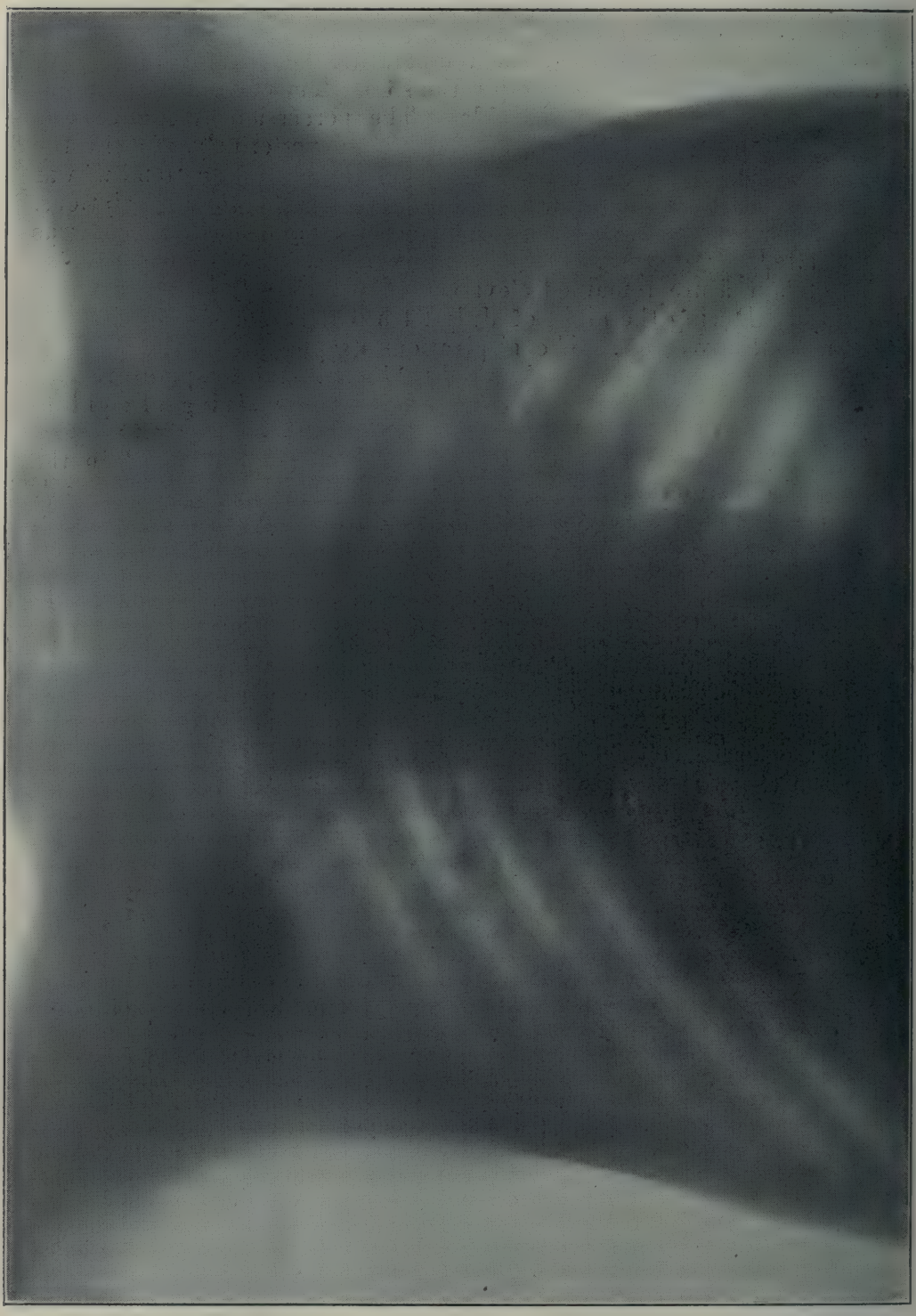


Fig. 1.

Before operation.

but became faint in the axillary region. The pulse was feeble and almost thready; the breath gangrenous. The patient was delirious and had to be restrained. Dr. Wood saw him with me at this time,

and agreed as to the advisability of operation. The man was transferred to the surgical wards, and, at my request, Dr. Pfahler made an

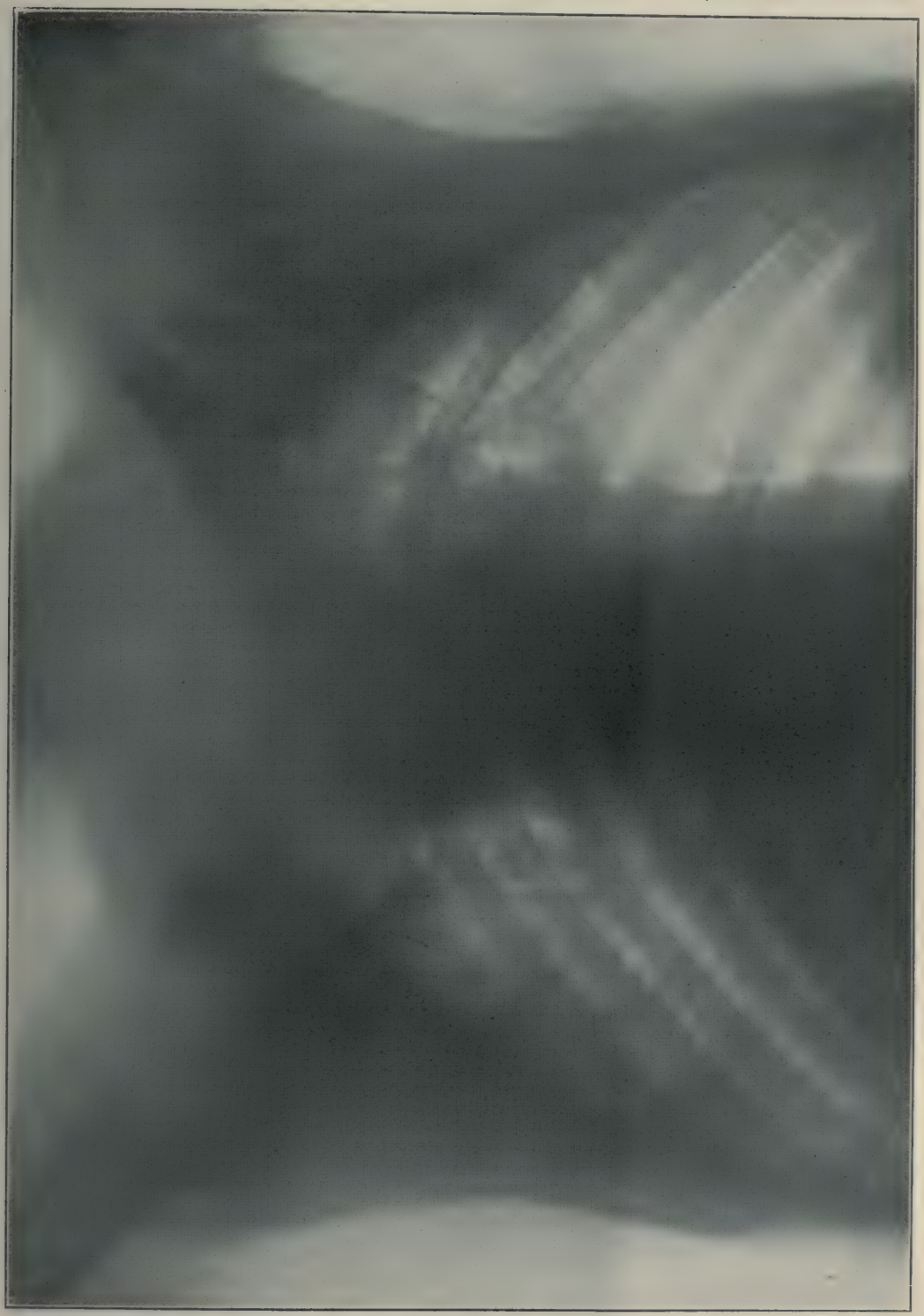


FIG. 2.

Several months after operation.

X-ray examination. Inspection with the fluoroscope showed impaired movement of the right half of the diaphragm, with a distinct shadow at the right apex. The lower portion of this shadow was on a level

with the base of the spine of the scapula. A negative was made, which was developed while the patient was being etherized and prepared for operation. This negative exhibited more distinctly the area involved, and showed a dense wall surrounding a lighter area in the upper part of the right lung. The lower portion of this wall was on a level with the base of the spine of the scapula, and apparently included all the lung space above this point. The patient moved during the exposure, and thus spoiled what would otherwise have been a good negative. Physical examination just prior to the administration of the anæsthetic showed, as before, a small patch of dulness and bronchial breathing in the area between the spine and the right scapula.

Guided by the physical signs and by the information furnished by the radioscopic examination, we were able to determine in advance where to make the incision and which rib to excise, the fifth being the one chosen.

The following are Dr. Wood's notes upon the case:

"I saw the patient referred to in the foregoing report through the courtesy of Dr. Riesman on July 28th last. The most striking feature was the very offensive odor that was observed upon entering the room, which became more pronounced as the patient was approached. The odor that came from the man's breath was typical of gangrene. The other features that impressed me were the normal temperature and the confused mental condition of the patient. The result of the physical examination is fully detailed above. I had no hesitation in coinciding with Dr. Riesman in the diagnosis of gangrene of the lung, and in the opinion that an early operation should be performed. The only point that seemed in doubt was whether the patient would survive the operation, but, as we felt that recovery was impossible by any other means, we considered it proper to give him this chance.

"The gangrenous area of the lung had been very carefully outlined by Dr. Riesman and Dr. Pfahler, and the latter had taken an excellent skiagram, which fully confirmed the location of the lesion as previously determined by physical examination.

"The operation was performed July 29th. Just before the anæsthetic was administered, Dr. Riesman again, at my request, outlined the area of dulness, which was on the level of the fifth rib, on the right side posteriorly, between the inner border of the scapula and the spine.

"Chloroform was administered until anæsthesia was complete, when ether was substituted. The skin was then cleansed in the usual manner, and the fifth rib exposed by a slightly curved incision, an inch and a half or two inches of it being resected by the subperiosteal method. The visceral and parietal layers of the pleura were found to be adherent, and dark and lustreless in appearance. The gangrenous portion of the lung was found to be just beneath the pleura, so that no delay or difficulty was experienced in reaching it. Some fragments of necrotic lung-tissue were removed. Digital examination showed the cavity to be as large as a man's clenched fist. It was not thought proper to irrigate the cavity, but the walls were gently cleansed with the aid of gauze sponges, which brought away all loose dead matter. The cavity was then packed with sterile gauze, and the usual dressings were applied.

"The patient bore the operation very well, and did not seem any worse in consequence. The wound was redressed daily, the packing and any sloughs that appeared being removed, after which fresh packing was introduced. The discharge was very profuse at first. The breath rapidly lost its foul odor, and, although the wound remained very offensive for some time, it gradually lost this character. The delirium persisted for some days, but became less and less pronounced, and finally disappeared entirely.

"Instead of a subnormal temperature, which was present before operation, the temperature rose immediately, reaching 101°. The pulse was 112 on the evening of the operation. On the fourth day the temperature reached 102.6°, pulse 104. From this time both temperature and pulse gradually declined. Cough continued to be a prominent symptom, but became less troublesome. The general condition of the patient changed for the better in a very satisfactory manner.

"While dressing the wound it was noted that air was expelled violently when the patient coughed, showing that a rather large bronchus opened into the cavity. The volume of air thus escaping from the wound diminished continuously as the cavity healed."

On August 24th a note says: "Patient still has cough, but otherwise is in a fair condition. Air still comes through the wound, but the probe shows that the cavity is decreasing in size. The patient feels well and wants to sit up."

From this time on the convalescence was rapid and satisfactory.

Some of the points of interest brought up by this case are, first, the use of the X-ray as an aid in locating the pulmonary lesion. While the procedure is no longer new, another instance of its value is worth recording. Although the skiagraph confirmed the physical signs accurately and in no way modified the treatment, it was very satisfactory to have this confirmatory evidence. It must be admitted that physical signs are sometimes misleading, and it is in these cases that the X-ray gives invaluable service. Tuffier (*Revue de Chirurgie*, August, 1901) advises that, when skiagraphic findings do not coincide with the results of auscultation and percussion, the latter be ignored and the operation be done according to the evidence furnished by the former. He cites a case in which the skiagraph showed a lesion toward the base of the lung, while the stethoscope indicated a higher site. The incision was made at the point indicated by the stethoscope with negative results. The next rib below was then resected, and the focus was discovered in the place shown by the X-ray. The same author reports eight cases in which he has applied radiography to pulmonary affections. The results were extremely satisfactory in five instances and negative in three. In some pathological conditions the X-ray fails entirely, but gangrene of the lung has been found to cast distinct shadows. In accepting the X-ray evidence, it is necessary to be assured of the fact that the plate is satisfactorily clear. If doubt exists it is better to discard it altogether. In order to be as certain as

may be, it is desirable always to have two skiagraphs taken, and to note whether they conform with each other.

The importance of definitely locating a lesion of the lung before undertaking any operative procedure will appeal to everyone. On this point Tuffier states that operations on the lungs when the lesion was accurately diagnosed beforehand were successful in 71 per cent. of the cases—that is, that the mortality was 29 per cent., while the mortality was 60 per cent. in the cases in which there was a mistake in the diagnosis. Of 300 cases collected by this author, the lesion was incorrectly diagnosed in 48.

The resection of a rib may be done under local anæsthesia if the condition of the patient will not warrant the use of a general anæsthetic; but in our case the delirious condition of the man made him an unsuitable subject for the former. When a general anæsthetic is necessary, chloroform is usually to be preferred.

The resection of ribs and the pleural opening should be ample in cases of pulmonary gangrene. This is more essential in these cases than in abscess of the lung, as the healing process is slower and it is necessary to keep the external opening patulous until the cavity is entirely closed. With a liberal opening, also, the wound may be drained with gauze, which I believe to be more efficient and suitable in these cases than tubes.

When the parietal and visceral layers of the pleura are adherent the lung may be opened immediately, but all operators agree concerning the desirability of securing this condition before attacking the lesion. When adhesions do not exist, therefore, the two layers should be stitched together around the proposed opening into the lung, which may be made at the end of forty-eight hours or sooner, if the patient's condition demands earlier relief.

Some operators advise against irrigating the cavity in these cases, and with these I am in entire accord; others are equally convinced of the value of this procedure. Those that hold the latter view should follow the method advised by Cotterill: "The fluid should be a mild antiseptic (not carbolic lotion); it should be warmed to about blood heat; it should be injected slowly and without force, great care being taken that it runs out as fast as it runs in. The patient should be rolled over into such a position that it is impossible for a large volume of the lotion to collect in the chest at one time, and, by its weight, embarrass the heart. . . . . The fluids I prefer to wash out with are: boric lotion, a solution of creolin, or a solution of izal, the latter of which is a particularly useful deodorizer."

Herezel states that about one-fourth of all the recorded operations upon the lungs have been for gangrene. Of 91 cases of pneumonotomy for gangrene, 60, or 61 per cent., were successful. Garré reports 122

cases operated upon for pulmonary gangrene, of which 66 per cent. were cured. He states that but 20 or 25 per cent. recover without operation.

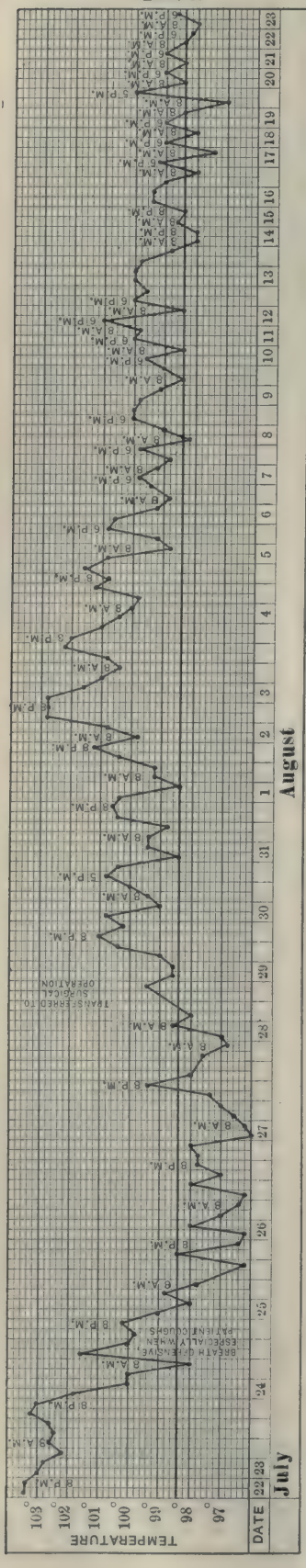
The patient's present condition is most satisfactory. He feels strong, his mind is clear, and he has become a useful helper about the ward. Physical examination shows a slight depression below the right clavicle. The percussion-note is the same on the two sides in front, but it is slightly impaired in the right axilla and below the operative wound for a distance of one and one-half inches. Auscultation shows increase in vocal fremitus, and harsh breathing in the neighborhood of the wound—not extending more than an inch above this. The urine has a specific gravity of 1018, and contains a faint trace of albumin, but no casts. The man has gained between thirty-five and forty pounds in weight. There is a slight discharge from the sinus, but the indications are that it will soon be closed.

While the chief interest of this case centres in the happy results of the operation performed by Dr. Wood, there are several points of importance to which brief allusion will not be out of place. The first of these is the cause of the gangrene. The history of an acute onset during fair health, with chill, cough, and pain in the side, suggests that the primary condition was lobar pneumonia. The question why this so rapidly—apparently within less than ten days from the time of onset—passed into gangrene cannot be answered except in a speculative way. It must be remembered that the patient had pronounced arteriosclerosis and albuminuria, and it is admitted by all that such conditions favor the development of gangrenous processes in the lung.

Lobar pneumonia is an accepted precursor of gangrene; but Aufrecht,[1] among 1501 cases of pneumonia, did not find a single case of gangrene—a most remarkable circumstance. He also cites Grisolle, who, in a collection of 305 cases of pneumonia, found none followed by gangrene, while among 70 cases of pulmonary gangrene there were only 5 in which the condition supervened upon pneumonia. Osler,[2] however, observed gangrene three times in 100 cases of pneumonia (3 per cent.); and in Norris'[3] collection of 500 cases from the Pennsylvania Hospital, there were three instances of gangrene—a proportion of 0.6 per cent. Tuffier,[4] in his collection of 74 cases, found pneumonia to be the etiological factor in more than 30, while Pomeranzew[5] found 5 cases of gangrene among 727 cases of pneumonia.

In the only other case of gangrene that has come under my own observation—one that I did not see during life, but upon which I made the autopsy—the condition also followed lobar pneumonia. Other causes of gangrene that need merely be mentioned are embolism, the aspiration of foreign bodies and of putrid material from the upper air-passages, wounds of the lung, tuberculosis, and the rupture of an empyema into the lung. Embolic gangrene has been observed after

FIG. 3.



abdominal operations in puerperal sepsis, as a sequel to middle-ear disease, and secondarily to other abscesses and pyæmic foci. The fetid material that is the cause of aspiration-gangrene may come from the pharynx, from the œsophagus in cases of obstruction or rupture, or, as in a case reported by Packard and Le Conte,[6] from a bronchiectatic cavity. Gangrene also occurs as a rare effect of compression by aneurisms or tumors. Diabetes, typhoid fever, alcoholism, and—according to Gee and Herringham[7]—scurvy, are predisposing causes of gangrene. It is probable that in the majority of cases of gangrene, the system at large or the lung itself was previously in a state of lowered vitality.

The second point that I desire to emphasize is the absence of fever in our case. Fever, according to the majority of writers, is an important symptom of gangrene. Aufrecht[8] states that he has never seen it absent. Usually it is high—40° C. (104° F.) and over. At times it is remittent. As the temperature chart shows, the gangrene in our case pursued its course, not only without fever, but with a subnormal—almost a collapse—temperature. Pulse and respiration were equally unsuggestive of serious trouble, and it was only the man's general condition, his delirium and prostration, that made us realize that he was in grave danger. At the Philadelphia Hospital the opportunities for observing anomalous types of acute pulmonary disease are abundant. Only recently I saw a case of complete pneumonic consolidation of the left lung, typical at autopsy, and complicated with purulent pericarditis, in which there had been no fever.

The third point worthy of mention is the character of the sputum. As stated in the notes of the case, there was no elastic tissue, and fatty acid crystals were likewise absent. The odor, however, was characteristic of gangrene. In the diagnosis of pulmonary gan-

grene the sputum deserves careful attention. In typical cases it separates into three layers, the lowest consisting of globular masses with a tendency to confluence, the highest being frothy and having masses of dirty sputum depending from the surface. The intermediate stratum is composed of a greater or less quantity of turbid, opaque fluid. When a part of the bottom layer is boiled with a 2 per cent. solution of potassium hydrate and examined microscopically on a slide, wavy bundles of elastic tissue are commonly found; but elastic tissue may be entirely absent. This fact is explicable on two grounds: first, the gangrenous process may have been arrested, the cavity no longer spreading, and, secondly, the elastic tissue may have been dissolved by the peptonizing action of the fluid—a result that is probably due to bacterial activity. It has been shown by Müller and by Simon,[9] to quote an analogous phenomenon, that the pneumonic exudate is dissolved by a proteolytic ferment. The fatty acid crystals are frequently absent. They are usually found in old cases of gangrene; ours was, of course, acute. In some cases of gangrene the sputum presents nothing peculiar, and the destructive process in the lung is discovered only at autopsy.

An attempt has been made to differentiate the odor of fetid bronchitis from that of gangrene. Aufrecht compares the former to the smell of stale cheese, and the latter to that of the fluid of manure.

It is scarcely necessary to discuss the other diagnostic features of gangrene. The sputum and the fetor of the breath are, as Osler[10] says, the distinctive features. The important point is accurately to locate the involved area. When the gangrenous process is circumscribed physical examination usually renders this possible; it serves at least to focus attention upon a particular spot in the lung. When, however, the process is more or less diffuse or the foci are multiple, accurate delimitation is difficult. In the circumscribed form there may be the signs of a cavity or those of consolidation. When the symptoms are clear and physical examination gives but dubious results, a careful search should be made for the presence of râles, as their detection may be the only clue to the situation of the trouble. Errors are, however, frequent. Strange to say, the physical signs are likely to locate the focus either too high or too low; the latter is more often the case. Furthermore, they do not give an exact idea as to the depth of the gangrenous area beneath the surface of the lung, and they often fail to map out its actual size. Usually the gangrenous cavity is found to be much larger than was expected. Gangrene has occasionally been mistaken for empyema, as in a case reported by Körte.[11]

Exploratory puncture naturally suggests itself as an aid in diagnosis and localization, but, on account of the danger of causing infection of the pleura with consequent empyema, or by carrying the needle that

has been infected by its penetration of the cavity into a healthy part of the lung, of producing a spread of the infection throughout the lung, exploratory puncture is better avoided. It is condemned by Lenhartz,[12] by Tuffier,[13] and also by Terrier and Reymond ;[14] the last-named authors think it permissible only as a prelude to operation.

Schulz[15] states that it ought not to be used while the thorax is unopened, but considers it one of the most valuable methods for locating the diseased focus after the thorax has been opened.

As has been pointed out by Dr. Wood, the X-ray is of great value in the diagnosis, as it usually indicates with fair precision the size and position of the gangrenous focus. Depending upon whether the cavity is full or empty, there will be either a dark shadow or a light area in the affected region of the lung. In addition, fluoroscopic examination will show a lessened mobility of the diaphragm on the diseased side. I would suggest that in hospitals in which radiographic examinations can be made with facility, every case of acute lung trouble in which abscess or gangrene is a possibility be subjected to such an examination.

Prognosis. In acute forms of gangrene the prognosis is better than in those that are chronic. Metapneumonic gangrene has a decidedly larger percentage of recoveries than has gangrene due to embolism, aspiration, or bronchiectasis. In Tuffier's table of 71 cases, showing the relation of etiology to results after operation, there were 55 cases of gangrene following inflammatory affections of the lung, with 39 recoveries; 4 cases of bronchiectatic gangrene, with 1 recovery; 2 due to foreign bodies, with 1 recovery; 7 of the embolic variety, with 2 recoveries; 1 due to chest wound, with recovery; and 2 following perforation of the œsophagus, both ending fatally.

The mortality from gangrene without operation is necessarily very high—between 70 and 80 per cent. (80 per cent., according to Verneuill[16]). Under operative treatment the death-rate falls to 34 per cent., according to Garré and Sultan,[17] who have collected 122 cases, with 80 recoveries and 42 deaths. In Eisendraht's[18] series of 28 cases of pneumotomy for pulmonary gangrene, there were 20 recoveries and 6 deaths, with improvement in 2. One interesting feature alluded to by several writers is the apparently complete restoration of the diseased lung. In some cases reported by Lenhartz[19]—who has operated upon 25 patients for gangrene, 13 of whom recovered—physical examination and examination with the X-ray showed a perfectly normal lung where there had previously been a large gangrenous cavity. The author gives it as his opinion that there must be a re-formation of lung tissue. The second radiograph of our case also shows a restored lung. Whether there is a true hyperplasia of air vesicles or merely an enlargement of existing ones, it is not possible to say without other, especially experimental, data.

All writers upon the operative treatment of gangrene refer to the importance of adhesions. Their presence greatly increases the chances of a good result; their absence predisposes to pneumothorax and to the entrance of septic material into the pleura, with resulting empyema. Lenhartz advises that if the condition of the patient does not demand immediate pneumotomy, this operation should be performed in two steps, the lung being fixed to the chest wall at one time, and opened later. When, however, all the signs indicate that procrastination would be dangerous, it is best to open the lung without delay, care being taken to draw the organ into the wound and to stitch it, so as to guard against the occurrence of pneumothorax and empyema.

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ZOMOTHERAPY IN TUBERCULOSIS.

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Some months ago two French scientists, Richet and Hericourt,[1] announced most favorable results in the treatment of tuberculosis with raw meat or its juice. They began two years ago to publish their observations, and during the last year both have written glowing accounts of the efficiency of this treatment. They have long been experimenting upon dogs, endeavoring to find some curative agent for tuberculosis; but all to no avail until they began to feed their dogs exclusively upon raw meat. Their dogs, 129 in number, may be divided into three groups. The first, composed of 30, received no treatment; the second, numbering

58, was treated by different methods, while the third, 41 in number, was fed on raw meat. At first the amount was unlimited, but later they found that 10 to 12 grammes per kilogramme of body weight of the animal was sufficient. The first and second groups lived, on an average, 52 days, while the dogs fed on raw meat lived, on an average, 227 days; in other words, the period of life was very nearly five times longer in the dogs fed with raw meat. From their experiments they conclude that cooked meat in any quantity is inefficacious, that meat deprived of its serum is moderately efficacious, and that muscle serum is as efficacious as raw meat. Raw meat they found also to act prophylactically.

The explanation of the action of the raw meat, although discussed at the Paris Conference in 1900, is still unsettled. Richet at that time attributed the beneficial effects to some body in the meat-juice that prevented the development of tuberculous granulations. According to Maragliano, meat acts as a stimulant, and therefore promotes the formation of an antitoxin in the body. More recently Richet has advanced a "metatrophic antitoxic action." The tuberculized animal, he says, dies by a slow and progressive intoxication of the nervous system. The active elements of the muscle serum preserves the nerve cell from a tuberculous intoxication.

Richet and Roux[2] have obtained favorable results in experimental meningeal tuberculosis in dogs. Twenty dogs were inoculated with tubercle bacilli in the spinal canal between the atlas vertebra and the occiput. Eleven of these were fed on raw meat and three survived, two of which were injected with tuberculin and did not succumb, as did one of the dogs which survived after being fed on cooked meat. Nine dogs were fed on cooked meat, and all died.

Chantemesse,[3] who first looked upon raw meat as a stomachic, has later taken an opposite view on account of his own observations. He injected two dogs with tubercle bacilli. One he fed upon raw meat; the other with cooked meat. The first remained sound and well; the second died.

Salmon[4] divided a number of dogs into three groups. The first, which received raw meat and was then injected, died as quickly as the controls. A second group, injected and then fed on raw meat, gained in weight and lived a fairly long time. In the third group treatment with raw meat was not begun until the disease had advanced considerably, and there was much loss of strength. On these raw meat exerted no influence. This author also calls attention to the fact that a dog which has apparently recovered from tuberculous peritonitis may still show at autopsy numerous fresh nodules in the peritoneum and internal organs and an extending tuberculosis.

Fränkel and Sobernheim[5] have published their results obtained by zomotherapy in tuberculous dogs and rats. Nine dogs and four rats

were injected with carefully estimated quantities of an emulsion of tubercle bacilli. Four dogs and two rats, fed on a mixed diet, were used as controls, and the remainder fed on raw meat. The dogs all died in six weeks. These authors suggest that Richet and Hericourt's results may be due to the fact that a non-virulent tubercle bacillus was used in the injections.

The literature on zomotherapy in human tuberculosis is more extensive, but no more conclusive. Duhoureau[6] mentions the case of his son, who, from smaller doses than those given by Hericourt, derived much benefit. Hericourt advises 600 to 700 grammes of raw meat, or the juice of 1000 to 1500 grammes of raw meat, per diem. In a recent article Hericourt[7] has collected statistics in zomotherapy in human tuberculosis. Besides eleven cases treated by himself, he reports twelve cases treated by others. These cases may be tabulated as follows:

TABLE I.

Site of lesion.	Number of cases.	Healed.	Improved.
Lungs	16	15	1
Glands	2	1	1
Skin	1	1	
Spine	1	...	1
Knee	1	...	1
Peritoneum	1	1	
Meninges	1	1	

It is but natural that anyone acquainted with pulmonary tuberculosis should, if the cases have not been selected, regard these uniformly good results somewhat skeptically.

Hericourt quotes, in addition, several favorable reports. Dr. Petit-Clerc[8] mentions three cases in the second stage of pulmonary tuberculosis who recovered under treatment by raw meat and fresh air. Dr. Sarge[9] has seen a case of pulmonary tuberculosis in the third stage recover under zomotherapy. Garnault[10] reports two cases in the second and third stages of pulmonary tuberculosis who apparently recovered under raw meat and intratracheal injections of orthoform. Josias and Roux[11] have followed zomotherapy as treatment in six cases of pulmonary tuberculosis in children, three of whom were in the second stage and did very well, and three in the third stage, who did not do so well. Three cases of meningeal tuberculosis were treated without favorable results.

At present the prevalent opinion is that Richet's method is only a better means of offering nourishment and of enabling a larger quantity

of food to be given. The resistance of gouty persons toward tuberculosis is, Weber[12] thinks, probably due partly to the meaty food. He recognizes, however, that due proportions of vegetables and fruits are of great importance. In some cases a fair amount of butchers' meat will stimulate the appetite enormously for all kinds of food, and render digestion more vigorous. Meat albumin, in contradistinction to milk albumin, writes Ross,[13] quickly and readily manifests its better qualities in the early observable improvement in the sufferer, and the benefit so obtained is not so easily undone as in the case of casein albumin. The cause, he thinks, is due to the fact that the adult has more muscle, and so needs more muscle-juice, or the muscle-juice contains more iron. Possibly, he says, the meat-juice contains some antitoxic substance. Browning the meat, he thinks, has little effect upon the real properties of serum.

Myosin albumin returns a maximum of nutrient for a minimum of effort, peptonizes readily, and is promptly absorbed, throwing little or no stress and irritating overaction on the stomach. But Bernheim[14] warns us that the benefit of alimentation is not measured by the quantity of food ingested, but by the quantity digested. The raw-meat treatment of Richet and Hericourt is, in effect, really suralimentation, but suralimentation in such a form that the majority of patients can stand it. "When, under the pretext of recovering the albuminoids, one submits the tuberculous patient to an exclusive meat diet, when one declares the carbohydrates—vegetables, sugar, cereals, etc.—to be secondary, the patient is deprived of an element primordially essential to repair, is given only an insufficient diet of phosphates, has his hyperacidity increased, and in place of increasing the artificial arthritism, which would be of value, a state of affairs is favored which would increase the susceptibility to the bacillus."

On account of the great expense, but few patients can carry out the raw-meat treatment as suggested by Hericourt, who advises that the juice of six pounds of rare beef, free from fat, bone, and cartilage, be taken daily. However, smaller quantities can be used advantageously. Two patients who took the full amount for several months made good recoveries. In one of these the disease was advancing quite rapidly. Many patients have been given beef-juice extracted from meat slightly browned, and it seemed to exert a very beneficial but no specific action.

In reviewing the experimental work done on this subject one is struck, as Fränkel remarks, by its meagreness. Chantemesse, Salmon, and Fränkel are apparently the only observers to repeat Richet's work. Fränkel obtained opposite results, Salmon's results were inconclusive, while Chantemesse, from experiments upon two dogs, upholds Richet. For this reason at the suggestion of Dr. Trudeau, and largely under his guidance, the following experiments were carried out:

The five dogs mentioned in Table I. were each inoculated in the external popliteal vein on July 17, 1901, with 2.5 c.c. of a translucent emulsion of tubercle bacilli. The tubercle bacilli were obtained by Dr. Baldwin from the sputum of a rapidly-advancing case of pulmonary tuberculosis. Hesse's agar was used to isolate the bacilli from the sputum, and after one transplantation to sheep serum tubes of dogs' serum (Prince's, q. v. infra.) were inoculated and the cultures used when eight days old.

Two dogs, King and Queen, were chosen as controls. They were fed on a diet of cooked meat, milk, and scraps from the table, but no raw meat. The remaining dogs received nothing but fresh raw beef. The dogs at once began to show but little desire for raw meat, and but one gained weight. The controls appeared much brighter for some time. The wounds on the legs remained open in all the dogs except Jester and Prince, where subcutaneous abscesses were found.

Jester, an old pug, died sixteen days after inoculation. On autopsy a perforation was found in the first part of the duodenum. A specimen of tænia saginata was found at this point of the bowel and was held to be the cause of the perforation, which led to slight peritonitis and death, probably from shock. Tubercle bacilli were found in the spleen, which was moderately enlarged.

During the fourth week all the dogs began to show signs of disease. Twenty-four days after inoculation Page died. Autopsy revealed general miliary tuberculosis of the lungs, general lymphatic glandular enlargement. Tubercle bacilli were found in the lungs and spleen. King, one of the controls, suddenly became very ill and died on the thirty-second day of the experiment. Miliary tubercles were found scattered throughout the lungs, and at the apices they showed beginning necrosis in the centre. A few hemorrhagic infarcts were found along the anterior borders of both lungs, and one spot of consolidation, size of a filbert, was discovered on posterior of left lower lobe. The spleen was very large and almost diffluent, and a general glandular enlargement was present. Lung, liver, and spleen showed many tubercle bacilli, while a few were found in kidneys, glands, and a cheesy focus in small intestine. The autopsy of Prince, who died on the thirty-fourth day, showed same condition in lungs and spleen, where a few scattered tubercles were seen. Enlarged glands, liver, spleen, and kidneys showed tubercle bacilli. The second control and last dog to die was Queen. The disease in the lungs had advanced further and conglomerate tubercles were found. Both lower lobes were nearly airless. The spleen was not so large as in the preceding dogs, but many miliary, grayish nodules were seen on section. Enlargement of glands was present. Tubercle bacilli were found in all the organs except the heart muscle. The heart's blood contained a few tubercle bacilli, but vast numbers were found in the liver, whose substance presented, on section, a peculiar translucent appearance, with a number of brown points surrounded by a narrow, yellow zone.

From this it is seen that the lungs and spleen bear the brunt of the infection, and that there was no greater difference between the pathological findings in the control and tested animals than among the tested animals.

The average life in the controls was thirty-four and one-half days; in the dogs fed on raw meat, it was thirty-one and one-half days.

TABLE II.

No.	Breed of dog.	Weight in kgr.	Quantity injected.		Injected July 17, 1901.	Food.	Death.	Days after injection.	Autopsy.
			Total c.c.	Per kgr. c.c.					
1 King.	¾ Spaniel.	11	2.5	0.22	Intravenously.	Mixed diet.	Aug. 18, 1901	32	Miliary tuberculosis of lungs; acute spleen tumor; tubercle bacilli from organs.
2 Queen.	Part Collie.	11.8	2.5	0.21	Intravenously.	Mixed diet.	Aug. 23, 1901	37	Miliary tuberculosis of lungs: tubercle bacilli from organs.
3 Page.	Mongrel.	9	2.5	0.27	Intravenously.	Raw beef.	Aug. 15, 1901	29	Miliary tuberculosis of lungs; tubercle bacilli from organs.
4 Prince.	Part hound.	17.3	2.5	0.14	Intravenously.	Raw beef.	Aug. 20, 1901	34	Miliary tuberculosis of lungs and spleen; tubercle bacilli from organs.
5 Jester.	Pug.	15.6	2.5	0.16	Intravenously.	Raw beef.	Aug. 2, 1901	16	Acute peritonitis; perforation duodenum; tænia saginata; tubercle bacilli from organs.

TABLE III.—WEIGHTS EXPRESSED IN PERCENTAGE OF NORMAL WEIGHTS.

Name.	July 17.	July 24.	July 31.	Aug. 7.	Aug. 15.	Aug. 22.	Aug. 29.
King	100	92.4	88	87	87	Dead	
Queen . . .	100	105.6	102	98	92	82	Dead
Page	100	100.6	96	92	78	Dead	
Prince . .	100	95.2	86.6	82	70	Dead	
Jester	100	96.2	86.4	Dead			
Average of controls	100	99	95	93	89.6	82	0
Average of tested	100	97.3	89 7	87	74	0	

Fearing that the tubercle bacilli used had been too virulent and that the dose given was too great, it was decided to repeat the experiment, using the attenuated tubercle bacilli grown by Dr. Trudeau for nine years under the name of R. 1. These tubercle bacilli are much attenuated, and injected subcutaneously in fairly large doses into guinea-pigs kill them only after many months. Accordingly on the 6th of December, 1901, six dogs were injected in the external saphenous vein with 2.5 c.c. of an emulsion of these attenuated bacilli. The dogs were divided into two groups. Four were fed on raw meat and given at the same time some fat and occasionally a little bread and dog biscuit. The two others were fed on a general diet exclusive of raw meat. The dogs, which had been fed well for some time previously, were all in good condition. Of the two chosen for controls, No. 5 was not in the condition of the other dogs, and shortly after the injection had a slight cough

which, however, soon cleared up. The dogs 1 to 4 inclusive gained weight for one week. Dogs 5 to 6 lost weight for a week, but then began to gain, and from that time on were in excellent condition and showed no loss of appetite. As seen from Table IV., dogs Nos. 3 and 4 died on the eighteenth and seventeenth days, respectively, after inoculation.

Their relative weights can be seen from the table. Dog No. 3 at first lost weight, but later gained considerable weight, and when he died, on May 4, 1902, 121 days after inoculation, weighed twenty-six pounds.

The last dog of the first group to die was No. 1, three-quarters Collie. This dog steadily gained weight for some months, but in July began to suffer from loss of appetite and refused to eat the raw meat. It was fed to him by hand for a time, and when he refused to eat it at all he was put on a general diet. Under this treatment he seemed to improve for a time, but later refused to eat anything but milk. He died finally on the 17th of August, 1902, 255 days after inoculation.

The two dogs used as controls after losing weight slightly at first began to gain. They never lost their appetite and were fed chiefly on "scraps from the table." Their weight never fell below normal, In August, 1902, both were subjected to the tuberculin test. Dog No. 5 reacted to 25 mgr. of Koch's tuberculin. Dog No. 6 received 25 and then 50 mgr. of Koch's tuberculin, but failed to react. This dog appeared well until about September 23, 1902, when he began to limp on his right fore foot. Two days later, after suffering for a part of one day from considerable dyspnœa, he died quite suddenly. The autopsy revealed a fibrous mass which had perforated (?) the aortic arch at the orifice of the innominate artery. A thrombus was found adherent to the aortic wall at this point.

On October 23, 1902, dog No. 5 died after showing slight signs of illness for several days. The left kidney was much enlarged, and the right kidney was the size of a small peanut and very sclerotic. The condition of the heart was similar to that found in dog No. 6, except that the acute endocarditis had more seriously damaged the aortic valve, which consisted largely of masses of vegetations. The mitral valve was slightly thickened, but not ulcerated.

From these figures it is seen that the test dogs lived on an average 110 days after inoculation and the two controls on an average of 308 days.

From the foregoing experiments on the treatment of experimental tuberculosis by raw meat, the following conclusions may be drawn.

1. That raw meat has no perceptible effect on the duration of experimental tuberculosis in dogs if the bacilli are virulent and a sufficient number injected intravenously.

2. That raw meat has no effect on the prolongation of the duration of experimental tuberculosis in dogs, even if the bacilli are attenuated, provided a reasonable quantity be injected intravenously.

3. That under the same conditions dogs fed on a mixed diet with no raw meat may live a much longer time.

Regarding the use of meat in pulmonary tuberculosis, it may be said:

1. That meat is highly essential in the dietetic treatment.

2. That much meat with a judicious admixture of carbohydrates, fats, etc., is essential to the treatment.

3. That rare meat is better than meat well cooked.

4. That meat-juice is of great value in suralimentation, as myosin albumin is easily digested by most patients—even the dyspeptic, and it affords a "maximum of nutrient for a minimum of effort." (In a few patients meat-juice causes diarrhœa and meteorism.)

5. That meat-juice can be taken when patients can take no other form of meat, *i. e.*, when there exists a marked repugnance to all solids.

6. That the juice from raw meat seems slightly, if at all, more beneficial than the juice from meat slightly browned.

7. That the disadvantages of preparing and preserving raw meat-juice more than offset its advantages. (Patients who object to juice from raw meat will willingly take that from meat browned.)

8. That meat-juice is of value, as it can be administered in the form of jellies, ices, etc.

TABLE IV.

No.	Breed of dog.	Weight in kgr.	Quantity injected.		Injected Dec. 6, 1901.	Food.	Death.	
			Total c.c.	Per kgr. c.c.			Date.	Days after injection.
I.	¾ Collie.	19.3	2.5	0.13	Intravenously.	Raw beef.	Aug. 17, 1902	255
II.	½ Spaniel.	13.09	2.5	0.19	Intravenously.	Raw beef.	Dec. 26, 1901	18
III.	Mongrel.	11.14	2.5	0.22	Intravenously.	Raw beef.	May 4, 1902	151
IV.	Fox terrier.	9.09	2.5	0.27	Intravenously.	Raw beef.	Dec. 25, 1902	17
V.	Bull and hound	19.1	2.5	0.13	Intravenously.	Mixed diet.	Oct. 23, 1902	323
VI.	Pug and Scotch.	10.8	2.5	0.23	Intravenously.	Mixed diet.	Sept. 24, 1902	294

TABLE V.—WEIGHTS EXPRESSED IN PERCENTAGE OF NORMAL WEIGHTS.

No.	Dec. 8, 1902	Dec. 15, 1902	Dec. 24, 1902	Feb. 10, 1902	May 8, 1902	Sept. 20, 1902		Autopsy.
I.	100	102	109.8	115	116	Died Sept. 17, 1902	.....	Tuberculous abdominal glands, tuberculous nephritis and orchitis; endocarditis.
II.	100	103.9	100.2	Died	Dec. 26, 1901	.....	.....	Tuberculosis of lungs, hæmatoma of stomach; pregnant.
III.	100	93	78.3	65	Died 106	May 4, 1902	.....	Tuberculous nephritis, tuberculous pulmonitis, hemorrhagic pericarditis (tub.?); endocarditis.
IV.	100	102.8	96.1	Died	Dec. 25, 1901	.....	.....	Pulmonary tuberculosis; pregnancy; tubercle bacilli in glands, spleen and liver.
V.	100	97	102.5	115	107	107	Died Oct. 23, 1902	Acute tuberculous endocarditis; adherent tumor containing tubercle bacilli ulcerating into aorta.
VI.	100	95	.....	.....	100.5	100.5	Died Sept. 25, 1902	Thrombus in aorta at orifice of innominate artery overlying erosion of aortic wall; adherent mass on outer wall of aorta; endocarditis (tuberculous?). On teasing no tubercle bacilli were found.

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NOTES FROM THE THROAT DEPARTMENT OF THE PATHOLOGICAL LABORATORY OF THE MANHATTAN EYE AND EAR HOSPITAL.[1]

(*a*) A Rapidly Recurring Bleeding Polyp of the Septum Nasi Appearing Twice in a Woman, Each Time at the Seventh Month of Pregnancy.

(*b*) Papillary Adenomatous Hypertrophy of the Mucous Membrane of the Septum.

(*c*) A Cyst in the Lymphoid Tissue of the Pharynx.

(*d*) Effusion of Serum into the Nasal Mucosa in Coryza.

WITH REMARKS ON THE RELATION OF THESE LESIONS TO OTHER MORBID CONDITIONS OF THE NOSE AND THROAT.

By Jonathan Wright, M.D.,
of New York.

An experience with such work extending over many years has long impressed me, and with an ever-increasing sense of its importance, with the great desirability that, connected with every large nose and throat clinic, a laboratory should be established in which all tissues removed from the patients should be systematically examined under the microscope. This should be done by a person thoroughly familiar with all the clinical problems presented by the histories, which in each case should accompany the specimen. Very meagre results are to be expected from the perfunctory examination of such material by a laboratory recluse. He should be in constant and thorough touch not only with all the phases of the morphological appearances of the tissue, but

[1] Read before the Laryngological Section of the New York Academy of Medicine, March 25, 1903.

with the clinical phenomena which accompany them. The endeavors of two sets of men, each only familiar with the clinical or the pathological side, however conscientious and earnest may be their labors, will always be, and have of necessity always been, markedly devoid of practical results in the advancement of our knowledge of the diseases of the nose and throat.

One tendency which is to be noted in all such work retards very much the elucidation of many of the most important problems we have to deal with, and that is the tendency to preserve for examination only the tissue from strange and unusual or doubtful cases, many laboring under the sad delusion that a malignant growth must of necessity furnish the most interesting tissue possible to the microscopist for study. Now, nothing can be more erroneous. In the study of the diseases which affect special regions of the body the examination of malignant growths microscopically is only of subsidiary interest. The problems connected with these belong more properly in the domain of general pathology. To a less extent this is true of the other two so-called "grand processes," syphilis and tuberculosis. The careful study of the common inflammatory processes and the connection of these with the benign growths is of very much greater importance. So multifarious are the appearances that, as is the case with the human physiognomy, no two specimens, no two sections, are exactly alike. Hardly any two pieces of tissue give the same reaction to reagents. Nay, more; one may almost say that hardly any two microscopic fields present the same appearance. This latter is especially true if we except the lymphoid tissue, whose hypertrophy presents more uniform pictures, due to the greater homogeneousness and regularity of the tissue, the slight changes to be observed from the normal, and the few elements involved. To the clinician anxious to know whether he has to do with cancer, syphilis, or tuberculosis of the nose or throat, the differentiation possible by the microscope is of the greatest importance and interest; but in studying the gradations between the different phases of manifest chronic inflammations and the more problematical steps to a papilloma or a fibroma this is of little service. The comparison of the appearances in a hypertrophic and an atrophic rhinitis and the study of their identical tissue changes is, in the present state of our positive knowledge, of much greater importance. The only way to arrive at a solution of many of these problems is by the patient and repeated study of every bit of tissue removed from the nose and throat in the routine of the clinic.

As an excuse for bringing before you to-night much repetition of what I have said on former occasions, I may plead the continuity of work along the same lines carried on for many years. As time has gone on new experiences have added somewhat to the links of the con-

tinuous chain which binds together many apparently dissimilar processes. To exhibit these properly it is necessary to repeat much which may appear old to you, in order to say only a little which may be new to any of you. It is otherwise impossible to make any advance in our knowledge of the correlation of morbid processes and their connection with normal conditions. After all, it is rather egregious vanity than commendable modesty to assume that what one has formerly said or written has not been forgotten. As to the continuous chain I have alluded to, it will, of course, be understood there are many links still missing. It will also be understood that there is very little, indeed, I have to offer you to-night which has not been presented by others.

(*a*) A RAPIDLY RECURRING "BLEEDING POLYP" OF THE SEPTUM NASI APPEARING TWICE IN A WOMAN, EACH TIME AT THE SEVENTH MONTH OF PREGNANCY.

These growths are to be classed among the angeiomata. There is no special reason for the classification of them in a separate category as bleeding polypi, a term which was inaugurated ten years ago by Schadewaldt, Alexander, Scheier and others.[1]

I find on looking at my records I have examined eight of these histologically. Any growth of the septum, benign or malignant, is usually very vascular—*e. g.*, the sarcomata—and one is frequently at a loss to be sure that the round-celled infiltration, which is always a prominent feature in such a growth as I show you to-night, does not warrant the diagnosis of small round-celled sarcoma. The subsequent clinical history is the only sure criterion, and frequent recurrences often cause the observer much anxiety as to the ultimate outcome.

A great deal of work has been done to illustrate the connection, both anatomically and clinically, between the erectile tissue of the sexual organs and that of the nose. As a very singular instance of it, I may report this case, which has been under my observation for a few years, in which a bleeding polyp appeared repeatedly in the nose of a woman at the seventh month of pregnancy:

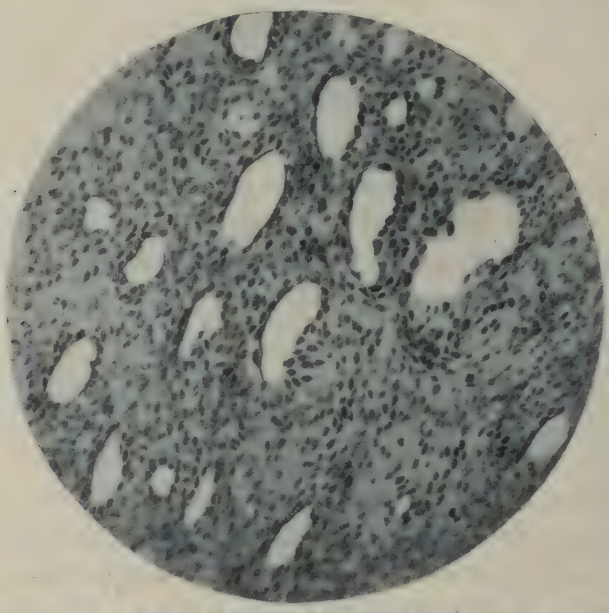
A woman, aged twenty-five years, came to the Brooklyn Eye and Ear Hospital on September 17, 1901, with a history of the septum having been burned several years previously for obstruction. From this there resulted a perforation. She had since been married and was then seven months pregnant. Springing from the perforation in the septum was a round, vascular-looking growth attached to the inferior and posterior edge of it. It rapidly recurred after extirpation, and on examination at that time showed nothing but very vascular granulation tissue. Recurrence a second time was larger than ever. It was then more radically removed, bits of underlying cartilage being cut away with it. That specimen showed some disordered cell structure and was richer in blood-

[1] Archiv. für Laryngologie, Band i. p. 259 et seq.

vessels than the tissue at the first examination. It was supposed to be an ordinary bleeding polypus of the septum.

About one year later (November 26, 1902) the woman again came with the history that the growth had not recurred noticeably after the last removal, shortly followed by the delivery of her child, born at full term and healthy, nor did she notice any discomfort until she had again become seven months pregnant, when she returned with recurrence of the growth, which now sprang chiefly from the inferior border of the perforation. It was of almost exactly the same appearance as the previous ones. This was removed and rapidly recurred. On December 17, 1902, it was again removed, and Fig. 1 represents the histological appearances.

FIG. 1.



The microscopic appearances of a "bleeding polyp" of the septum, recurring twice at the seventh month of pregnancy. Photograph × 10 (retouched).

On microscopic examination the tissue is seen to be covered by degenerated flat epithelial cells, under which there is a layer of what appears to be hyaline degeneration of the connective tissue. The mass of the growth is made up of loose œdematous connective tissue in which there are a large number of mononuclear round cells which take the hæmatoxylon stain very deeply, and the whole growth is traversed by very numerous capillaries lined by a single layer of endothelium whose nuclei are very much swollen and project into the lumina of the blood-vessels. There is every evidence of considerable inflammatory action, but no proof of the malignant nature of the growth.[1]

Whatever the subsequent history of the case may be, the rapidity with which this vascular growth recurred during pregnancy and its

[1] Since this paper was written this patient has been seen several times, first about three weeks after delivery. The growth was then the size of a pea. A month later it was the size of a grain of wheat, and a third time, still diminishing. Apparently, therefore, the growth had already recurred and grown to considerable dimensions in the two months elapsing between the last removal and the birth of her last child, and in the two months which had succeeded delivery it was as rapidly disappearing.

quiescence or absence at other times is, in view of the previous literature, interesting to say the least. The coincidence of the appearance of this growth and its repeated recurrence at the seventh month of pregnancy is one of the clinical facts which, though they cannot be very lucidly accounted for, nevertheless, taken in the aggregate, point to a more or less important relationship between the nasal and the genital mucosa. In another publication I have shown the anatomical differences in the nasal erectile tissue of the bull and the steer.[1]

From anatomical as well as from pathological and physiological facts we know there is a more or less indefinite sympathy between the erectile tissue of the nose and the genitalia. In order to elaborate some considerations connected with this subject, I will quote rather extensively from some work I published seven or eight years ago:[2]

"In the erectile tissue of the nose the larger arterioles well supplied with muscular coats lie in the deepest layers of the mucous membrane close to the bone. They give off branches which supply, by a network of capillaries, the periosteum, the glands, and the epithelial layer of the mucous membrane. These capillaries are collected into the veins, which dilate into venous sinuses, the larger lacunæ of which are the deeper, the superficial lacunæ or "cortical network" communicating with them. These lacunæ again empty into the veins which accompany the primary arterioles into the periosteal layer.

"Zuckerkandl says he has never seen the arteries emptying directly into the venous sinuses. The same was said for a long time of the corpus cavernosum of the penis, but they were finally conclusively shown to do so, and I am not convinced that this does not occasionally take place in the erectile bodies of the nasal mucous membrane, though I have thus far been unable to trace the connection between the two.

"The capillaries, usually at least, do not empty directly into the venous sinuses nor into the radical veins accompanying the arteries. They are usually seen collected first into veins. The smaller veins of the periosteal layer empty directly into the radical veins accompanying the arterioles.

"Nevertheless, by comparing all these different conditions the probable mechanism of the blood-supply in the highly evolved nasal mucous membrane of man becomes pretty evident. The radical arteries and veins pass through various bony canals into the nose, as the large sphenopalatine foramen and smaller foramina in the ethmoid. The artery will evidently compress, when dilated, its accompanying vein against the bony walls, thus letting in more blood and limiting the outflow.

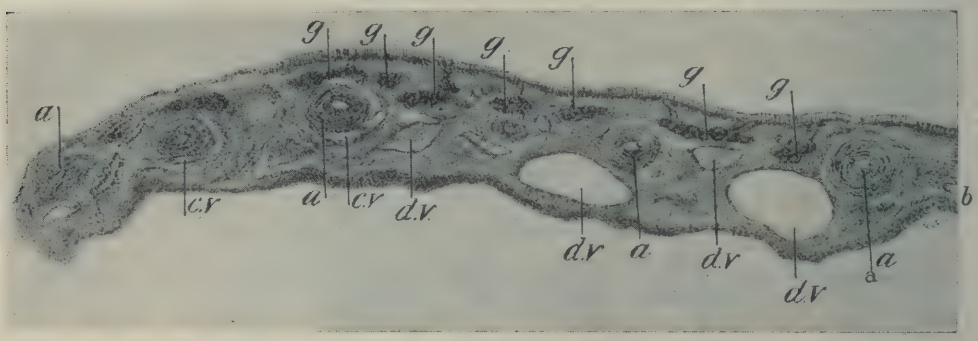
[1] New York Medical Journal, November 19, 1898.

[2] A Consideration of the Vascular Mechanism of the Nasal Mucous Membrane and its Relations to Certain Pathological Processes. THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, May, 1895.

Contraction of the artery acts in the inverse sense. This arrangement has been described for the blood-supply of the marrow of the long bones.

"There is a similar mechanism, as the arterial branches with their veins lie in the deep or periosteal layer of the mucous membrane. Fig.

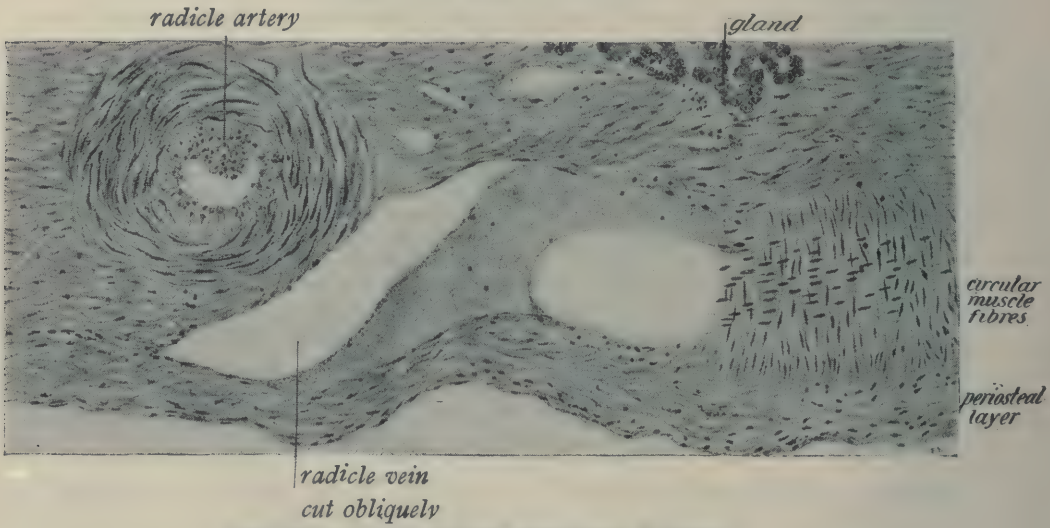
FIG. 2.



Nasal mucous membrane of sheep. *a*, artery. *b*, periosteal layer. *g*, gland. *d.v*, dilated vein. *c.v*, closed vein.

2 and Fig. 3 show very clearly how this occurs in the sheep. You will observe that many of the large veins lie between the very muscular arteries and the firm periosteum at the level of this particular section. Of the thirty or forty sections examined, this arrangement was evident

FIG. 3.



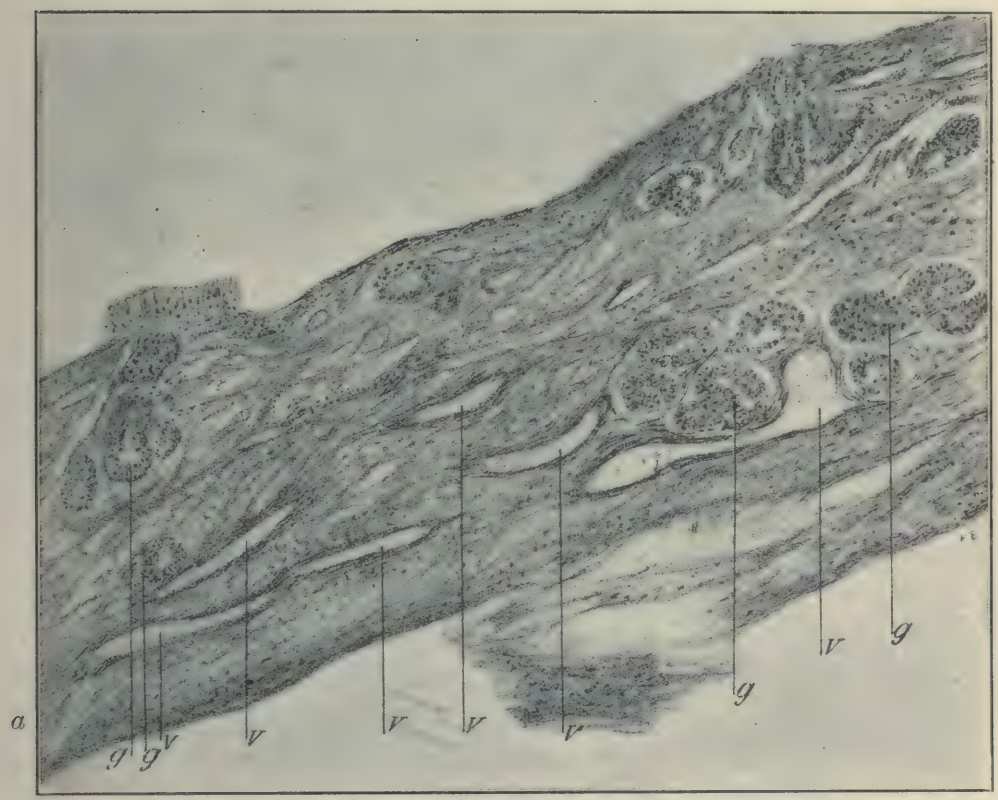
Deep layer of nasal mucous membrane of sheep.

in so many pairs that it is fair to presume that at some one or more points each radicle artery and vein stand in such a mutual relation that an increase in the diameter of the artery must result in an encroachment upon the lumen of the vein without entirely closing it. While this

drawing is from the mucous membrane of the sheep, the same arrangement, by careful study, will frequently be found in that of man (Fig. 4); but, owing to the very much more complex and irregular course of the vessels, it does not present such a striking and convincing illustration.

"There is such a complete anastomosis of the superficial veins with one another, with those of the skin at the edge of the nostrils, with the veins of the dura mater and of the orbit, that this obstruction to the venous return probably exerts its dilating tendency only or chiefly upon the

FIG. 4.



Nasal mucous membrane from septum of infant. *a*, periosteal layer. *v*, radicle vein. *g*, gland.

deep network of the erectile bodies. It does act, however, upon them as the supply and escape valve to the cavernous sinuses, and stands in the place of the muscles which compress the radicle veins of the penis and the clitoris."

Now this brings us to a point which is not sufficiently realized in nasal pathology. The nasal mucosa is a peculiar mucosa, differing essentially from all other mucosæ of the body in one very important particular. That is the presence immediately beneath it of bone structure in close relationship with its most important elements, the

bloodvessels and the glands. This is indicated at the level shown in the drawings by the periosteal layer. This relationship of the mucosa is still more peculiar in those thin lamellæ of bone, the turbinates, which are covered not on one side alone, but on both. I am obliged, however, to confess that I have not observed arterioles and veins in juxtaposition piercing these thin lamellæ through a common channel. As a rule they run parallel with these bony plates, and in the compression of the vein by the dilating artery, if they are a contributing part of the mechanism, they are non-elastic plates against which the compressible vein is apposed. This may be accomplished not only by the dilating artery, as I have hitherto urged, but by the contractile energy of the unstriped muscle fibres and the elastic fibres of the superimposed stroma. It is very probable indeed that compression of the glands also takes place and their contents are extruded by the same mechanism. Now this is the only mucosa in the body whose radicle bloodvessels are thus contained in dense unyielding channels, and the importance physiologically I have dwelt on in the extract I have just quoted. Not only must we bear this in mind when we consider the mechanism of the blood-supply of the mucosa, but it has an important bearing on our comprehension of various inflammatory processes. It doubtless is an important factor in the etiology of the unique lesion of atrophic rhinitis, and it probably is the cause of the frequency with which œdema supervenes in the chronic inflammation of the nasal mucous membrane, forming polypi or the so-called polypoid degenerations. We have œdematous polypi elsewhere, as for instance in the larynx, but the effusion of serum in growths elsewhere never reaches the degree observed in the nose. As for the lesion of atrophic rhinitis I quite agree with others that there are plausible reasons for believing that the essential lesion and the primary one in atrophic rhinitis is a bone lesion which interferes in some way with the radicle vessels which lie in bony canals, or are compressed in some way against bony plates.

(*b*) PAPILLARY ADENOMATOUS HYPERTROPHY OF THE MUCOUS MEMBRANE OF THE SEPTUM.

A number of years ago considerable discussion was elicited through the publication, by Dr. Hopman, of a large number of cases of what he called nasal papilloma, which many of us believed to be merely papillary hypertrophy of the mucous membrane of the nose, usually situated upon the inferior turbinated bones at their posterior borders, where we have regularly a large amount of erectile cavernous tissue. In several publications[1] I took the latter view with Chiari and many others. I believe it will now be conceded that this latter view has prevailed in nasal

[1] New York Medical Journal, December 26, 1891; October 13, 1894; December 14, 1895.

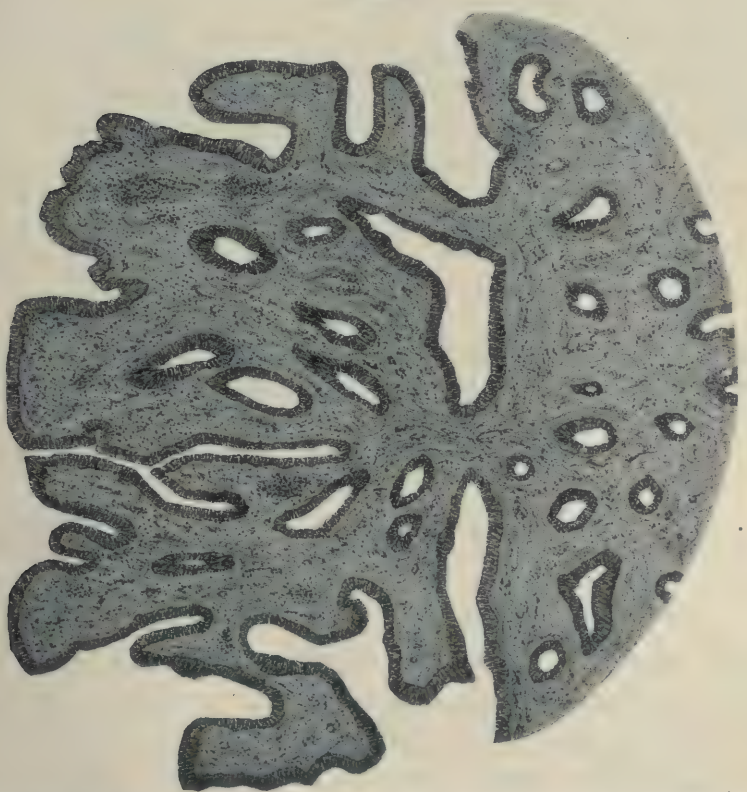
pathology. While these papillary hypertrophies are usually found in the situation I have mentioned above, the following case will illustrate that the same form of growth may occur under certain conditions else-

FIG. 5.



The reduplication of the surface epithelium in a papillary adenomatous hypertrophy of the mucous membrane of the septum. Photograph × 10 (retouched).

FIG. 6.



The hyperplasia and reduplication of the glandular epithelium in a papillary adenomatous hypertrophy of the mucous membrane of the septum. Photograph × 10 (retouched).

where. From the drawing (Figs. 5 and 6) made under low power it will be plainly seen that we have to deal with the reduplication of the surface and glandular epithelium of the septum. The method by which this takes place I have explained in a paper on "Papillary Œdematous Nasal Polypi and Their Relation to Adenomata."[1] I am indebted to the kindness of Dr. W. F. Dudley for this specimen and for the following history:

Man, aged thirty-five years. He had had nasal polypi removed from both sides of the nostril. Ten years ago he had an abscess of the frontal sinus, which ruptured spontaneously. A surgeon had enlarged the external opening and curetted the sinus. Since then he had been treated for nasal polypi in both sides of the nose, and also in the frontal sinus. This specimen, "a thickening," was removed from the right side of the nasal septum, anterior third, at the junction of the triangular cartilage with the vomer. The thickening was in contact with the floor of the nose. There was no pain, no glandular involvement, and but moderate bleeding. There was some thickening also of the septum projecting into the left nasal cavity. As frequently happens in these growths, there has been some recurrence since the operation.

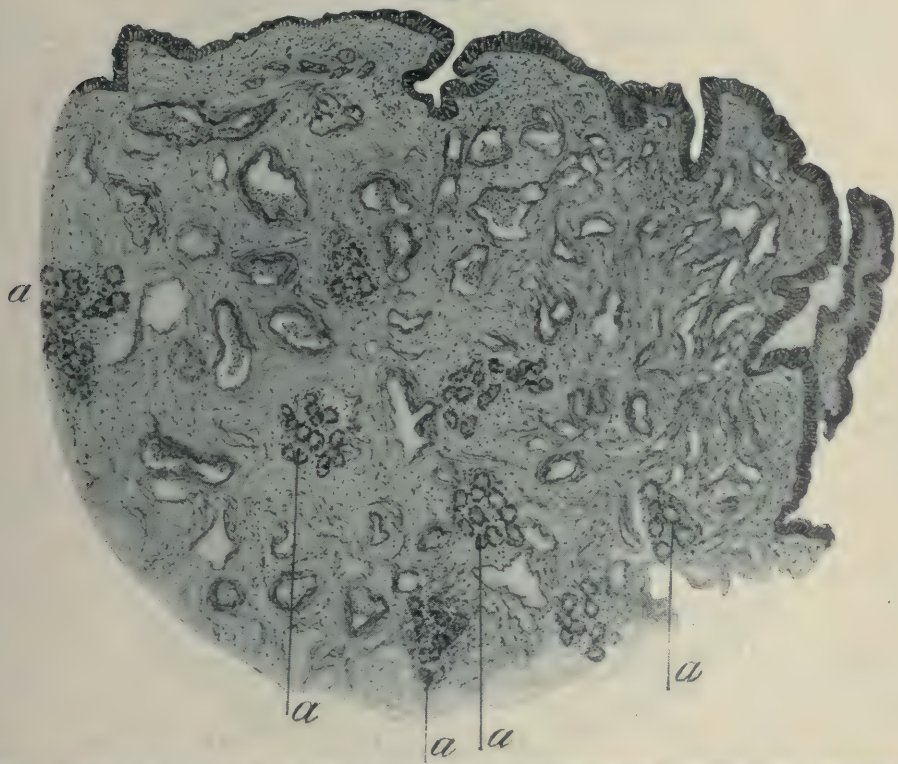
Microscopic examination shows under low power a very corrugated surface lined by a thin layer of columnar epithelium, giving it to the naked eye the appearance frequently seen in papillomata; but there is no real increase in the number of epithelial layers. The stroma is loose and œdematous, filled with mononuclear and a few multinuclear leucocytes, and a moderate number of capillary bloodvessels only slightly dilated, some of the walls being thickened in their fibrous coat, and the endothelium being usually swollen. The epithelium under the high power seems to be columnar in character, and there are in the sections a number of rings of epithelium, separated from the surface in the substance of the growth, evidently the walls of the acini of the hyperplastic racemose glands, cut transversely or obliquely. Some of these communicate with the depressions of the corrugated surface. The growth, except for the small number of bloodvessels, is very similar on its surface to those which are common at the posterior end of the inferior turbinated bones. The corrugation of the surface is largely due to the dilatation of the ducts of the glands, but also, I believe, to the lateral division of the surface columnar epithelial cells. The whole growth is to be looked upon as an exceptional instance, in the situation in which it was found, of œdematous papillary hypertrophy of the mucous membrane, which is becoming adenomatous.

During the preparation of this paper two specimens on the same day in sequence have come under my observation which illustrate some further points in the interrelation of these growths. Fig. 7 illustrates an ordinary papillary œdematous hypertrophy of the posterior end of the inferior turbinated body, the so-called "mulberry hypertrophy." Taking note of the unusually striking appearance of the dilated cavernous sinuses in this specimen, you will also observe the reduplication,

[1] New York Medical Journal, November 13, 1897.

the corrugation, or papillary condition of the surface. Now I believe that this epithelial hyperplasia is the essential one, and not the fibrous digitations which form the framework of it. At *a* I have had indicated somewhat schematically the condition of the racemose glands in this tissue. You will observe that there is relatively little change in these, saving some round-celled infiltration around them, the glandular epithelium being practically unaltered, and the lumina of the acini not being especially dilated. We may conjecture that the greater amount of fibrous tissue and the engorgement of the venous sinuses has by mechanical compression had something to do with the prevention of hyper-

FIG. 7.



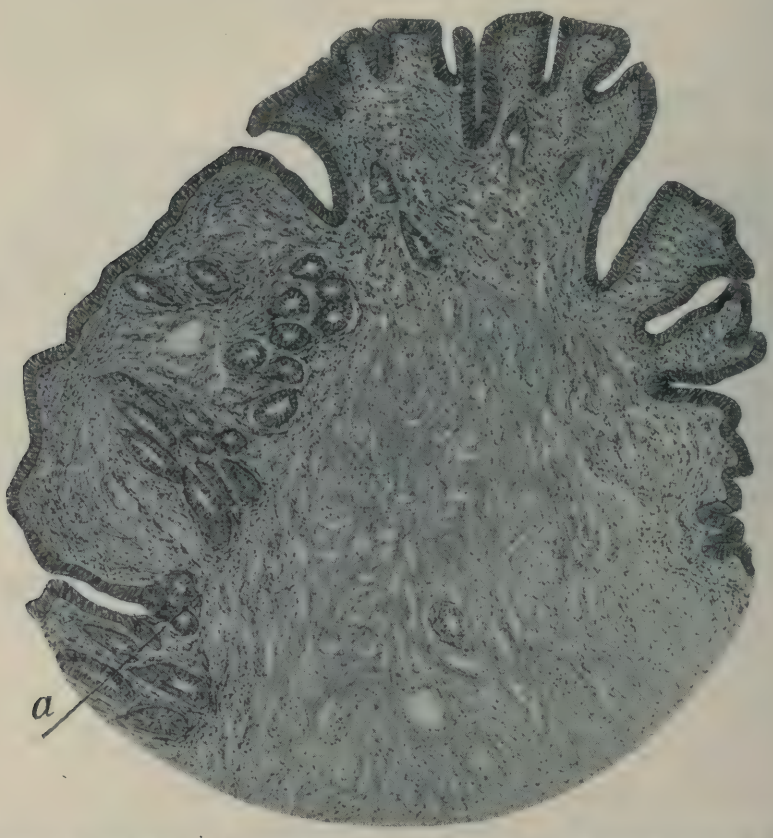
The structure of the posterior end of the inferior turbinated body, showing the hyperplasia of the surface epithelium and the dilatation of the venous sinuses. The glands are unaffected, but are here much exaggerated in size to show their presence. Camera lucida × 10.

plastic changes in the glands at this point in this hypertrophy. This is not always the case in this locality, for, as you will see in some of the lantern slides I will exhibit, this glandular hyperplasia is present in other specimens from this locality where the sinuses are not so prominent, but the point is still better illustrated in the other specimen referred to above, which is a papillary œdematous hypertrophy of the posterior end of the *middle* turbinal. Here, in this case, we have no venous sinuses at all, and you may observe in Fig. 8 the involvement of the glandular epithelium as well as that of the surface. This is an unaltered camera lucida drawing, which sufficiently illustrates the

point. In the former specimen we have the papillary condition of the surface only, in the latter the papillary condition of the surface *and* the adenomatous hyperplasia.

These growths are rather uncommon in the nose at a stage of exclusive adenomatous hyperplasia, but are thus much more frequently found in the rectum, the uterus and its adnexa, and in the bladder. In the sections which I exhibit (see Figs. 5 and 6) in connection with this septum case I think you will be able to note the relationship not only of

FIG. 8.



The structure of the papillary œdematous hypertrophy of the posterior end of the middle turbinated body, showing the involvement of the glands. At *a* is seen the dilatation of a glandular duct helping to make the papillary surface. Camera lucida × 10.

the ordinary hypertrophies of the posterior ends of the turbinate to this growth, which borders on the class of adenomata, but you will see from the sections that we also have the marked œdema of the stroma, which is the only characteristic of the ordinary nasal polyp. Were it not for this lateral cleavage in the columnar epithelial cell leading to reduplications and inversions of the surface and glandular epithelium, we would call the hyperplasia by the clinical term polypoid. In studying these growths we must remember that embryologically the racemose glands of the mucosa are normally nothing but the inversions of the

surface epithelium, and we conceive of these adenomata as being nothing but the morbid activity of the cells excited by some stimulus, which we have every reason to believe is usually a chronic inflammation. Now, a very interesting and a very mysterious phenomenon is the frequency with which what you here perceive is essentially a benign growth becomes a malignant adenoma. When in these adenomatous growths you find areas in which the cells are multiplying not alone in such a manner as to form tortuous loops of epithelium of one or two layers, but so that there are many layers which intervene between the lumina of the false acini or loops of columnar cells and the stroma, we may suspect that the tumor is putting on a malignancy which, however frequent the recurrence may have been, has hitherto been absent. Hitherto we have had to do with a surface hyperplasia. When malignancy commences a deep destructive infiltration begins which we know will eventually develop into all the clinical and morphological characters of cancer.

It is a very plausible assumption and an entirely possible explanation to say that these benign hyperplasias of epithelium furnish the proper soil and a nidus for the specific contagium of cancer, and that when this tissue becomes the abiding place for it, then the infiltration begins. However attractive this theory may be, it lacks all the necessary elements of scientific demonstration. There is even not enough accumulation of circumstantial evidence to render the theory anything more than a suggestive possibility. This is not the place to enter into a discussion of the germ theory of cancer. Recent investigation has fully demonstrated the unsatisfactory character of the evidence thus far presented, but we must remember that nothing has thus far been advanced to demolish the theory. It seems probable that we must await the development of higher resolving powers for our microscopes and for more sensitive chemical reagents, but we should also keep our minds in a more receptive condition as to the possibility of the independent existence of simpler entities than the animal cell. That is no longer a microcosm. It is a macrocosm. For a long time various morphological phenomena within the cell have been studied under the high powers of the microscope, and recently the astounding facts which have been elicited in the laboratory study of immunity have excited the minds of investigators to such an extent that already theories have been advanced to explain them, which future fuller knowledge is very likely to demonstrate as erroneous, or at least as premature. These are the chemico-biological aspects of the problem of intracellular life which are apt to be proven hereafter to have a decided relationship to the etiology of cancer.

(*c*) A CYST IN THE LYMPHOID TISSUE OF THE PHARYNX.

From time to time, for many years, I have been much interested in certain forms of cystic growths found in the nose and throat.[1] The retention cysts which form in the racemose glands are common enough[2] and well enough understood to deprive them of any special interest when found. Only less so are the so-called inclusion cysts, such as we meet with in the pharyngeal vault, called by Tornwaldt the pharyngeal bursa, being merely the space included by the agglutination of two contiguous folds of the mucous membrane. I have also met with this formation along the lateral walls of the pharynx.[3] It occasionally happens—at least I have once observed it—in the posterior ends of the inferior turbinated bodies when enormously hypertrophied, that the dilatation of one of the cavernous sinuses assumes the size of a cyst filled with blood. Besides this, the cysts forming in nasal polypi are not always due to the dilatation of glands which may be contained in the pendent tissue, but in rapidly forming polypi, and especially in those exceptional cases where the patient is younger than sixteen or seventeen years, are found cysts formed by the breaking down of the scanty stroma and the more abundant coagulated fibrin which goes to make up the framework of the polyp. Elsewhere I have drawn attention to this method of cyst formation as being allied to the formation of blebs by the effusion of serum just beneath the epithelium, this being frequently of neurotic origin.[4] But there is another form of cyst which is very rarely met with and always, of course, in the pharynx, and that is one formed *within* the structure of the lymphoid tissue. It results apparently from the dilatation of one or more of the lymph spaces through some cause which I cannot fully understand, as it would seem that impediment to the lymphatic circulation could hardly be so localized as to cause dilatation of the channels behind it. Whatever may be the cause, however, it is a fact that these cysts are occasionally met with. In the drawing Fig. 9, herewith produced from a section of a specimen kindly furnished me by Dr. Berens, this is especially well seen. It came from the glosso-epiglottic fossa. Apparently several contiguous microscopic lymph nodes embedded in the loose connective tissue were the seat of this method of cyst formation. In the drawing, at the larger end, may be seen a lymph node of which almost the entire calibre is taken up by the dilated lymph space, there being merely a rim of lymphoid tissue around the cavity. At the small end may be

[1] A Cyst of the Pharyngeal Bursa. Medical News, September 7, 1889.

[2] Some Remarks on the Structure of Œdematous Nasal Polypi. New York Medical Journal, November 4, 1893.

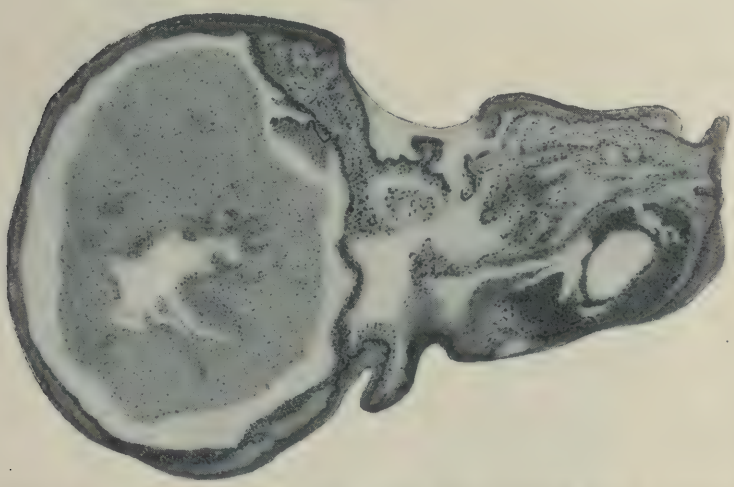
[3] A Cyst of the Nasopharynx and a Cyst of the Oropharynx. New York Medical Journal, 1895.

[4] Remarks on the Etiology of Nasal Polypi. Laryngoscope, 1899.

seen the beginning of another cyst which is forming in this manner, the encircling rim of the lymphoid tissue in this last case being relatively much larger than that of the cavity at the larger end. The case had no especially marked clinical history, except that of slight irritation of the throat.

There is some tendency to confound these rare cysts with the equally rare cases of abscess of the lymphoid tissue, and these two again with the retention plugs found in the lacunæ of the tonsil which have been sealed over in the process of inflammation. In the cases of true abscess,

FIG. 9.



Showing at the larger end of the drawing a lymph node whose area is almost completely occupied by a cavity lined neither by epithelial nor endothelial cells, but connected directly with the lymphoid tissue, while at the smaller end a similar cavity is observed with a thicker rim of lymphoid tissue. Photograph × 10 (retouched).

zones of inflammation and colonies of cocci, presumably pathogenic, may be found in the neighboring lymphoid tissue which has not yet broken down into an abscess cavity. In the retention cysts of the lacunæ we find either a complete coating of epithelium on the walls or a plainly recognizable remnant of it. In this specimen neither of these conditions are present and we have, I believe, a true lymphatic cyst.

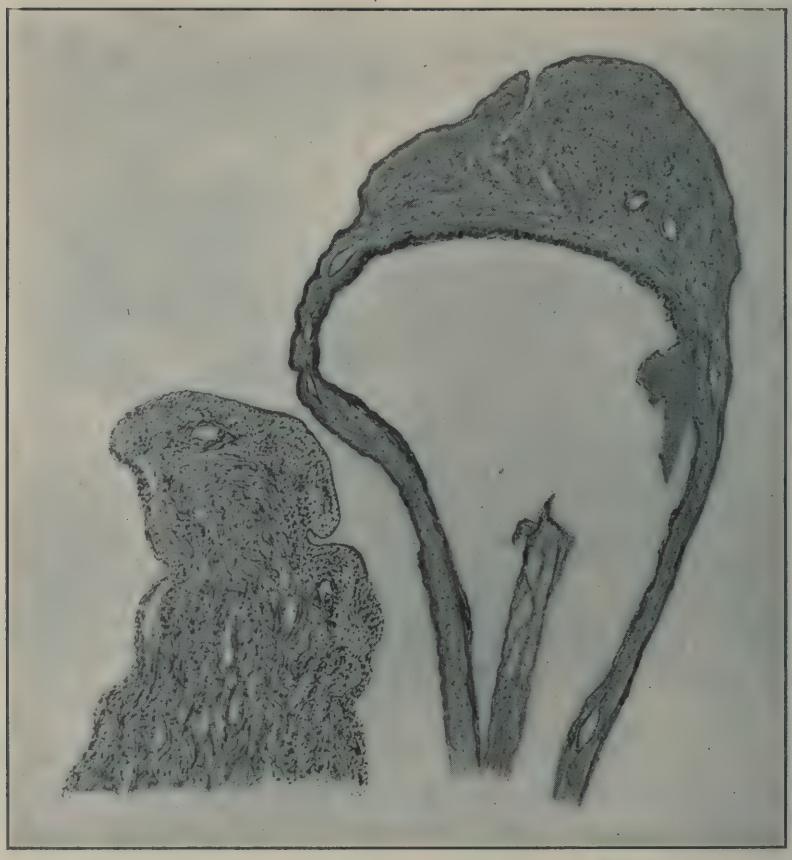
(*d*) EFFUSION OF SERUM INTO THE NASAL MUCOSA IN CORYZA.

Besides the cases of dilated spaces within morbid growths which I have mentioned and which are properly designated as cysts, we have in acute coryza, especially when affecting the already œdematous mucosa of the nose, a dilatation of the lymph spaces due to the sudden and excessive exudation of serum from the bloodvessels into the stroma weakened in the processes of chronic inflammation. This is illustrated in the drawing Fig. 10, taken from a section of the mucosa of a middle

turbinated body removed during the period of a coryza when the nasal passages are most completely occluded.

In a mucosa not too much altered by chronic inflammation there is still contractile power enough in the unstriped muscle fibres and in the elastic fibres of the stroma to temporarily drive out the blood during the attack from time to time, and, finally, on the subsidence of the

Fig. 10.



The dilatation of a lymph space or the separation of the fibres of the stroma of the nasal mucosa by the effusion of serum during the congestive stage of a severe coryza. Dimensions: 6 x 3 mm. Camera lucida × 10.

coryza to permanently squeeze out or cause the absorption of the serum. In a mucosa badly damaged as to the contractile energy of these elastic and muscle fibres, this ability of the mucosa to regain its normal volume temporarily and permanently is weakened, or has entirely disappeared in exact proportion to the amout of damage done by the previous long-standing chronic inflammation.

REVIEWS.

APPLIED SURGICAL ANATOMY REGIONALLY PRESENTED, FOR THE USE OF STUDENTS AND PRACTITIONERS OF MEDICINE. By GEORGE WOOLSEY, A.B., M.D., Professor of Anatomy and Clinical Surgery in the Cornell University Medical College; Surgeon to Bellevue Hospital, etc. Octavo, 511 pages, with 125 illustrations, including 59 full-page insert plates in black and colors. Philadelphia and New York: Lea Brothers & Co., 1902.

A CAREFUL examination of Dr. Woolsey's new book makes one feel that he has made an addition to medical literature of genuine value. Not that there is anything particularly new in surgical anatomy, and not that the author has more than kept pace with the advances of operative surgery, but it is a happy union of fact and practice, the latter based upon the former, which brings into distinct view the enhanced advantage that can be taken of this combination. The book bristles with good advice about many minor as well as more important essentials, and it is withal so entertainingly written that such advice is made to appear doubly welcome.

To speak more definitely of particular portions, we are tempted to criticise the rather meagre details which are given under the head of localization of cerebral functions. Surely a surgeon like the author might have described the method of Chiene, or the cyrtometer of Wilson, without stepping aside from his expressed intention, inasmuch as other and perhaps less simple methods of locating the principal fissures are given. An excellent instance of the applied anatomical method of diagnosis is afforded by the description of facial paralysis under the head of nerves of the head and neck. Mention is made of the anterior method of attack upon Meckel's ganglion, but not of the approach after lifting the zygoma. In the description of the nasopharynx, the anatomical arrangement of its adenoid tissue is briefly given, but the author has omitted to call attention to the fact that originally it forms a perfect collar of lymphoid tissue around the neck of an embryonic canal. He has made the same omission, by the way, in describing the appendix, whose origin from the cæcum is similarly arranged. These facts are of importance, because such tissue is extremely prone to succumb easily to infectious processes, which will explain the local disaster often seen in the throat and about the appendix.

His description of the cervical sympathetics is brief and not so full as one might wish, especially in view of the growing importance attaching to these nerve trunks and ganglia, in view of possible surgical attack upon them for at least three more or less common conditions. The writer does not like to complain of omissions, and yet he regards this book so highly that he would like to see it so complete and perfect in

all its parts that one need not refer to any other work upon its general subject.

The description of the cervical fasciæ, their various planes and compartments, is excellent and of great practical importance. When describing the branchial arches the author speaks of the first as forming the upper jaw, which is not our understanding of the embryology of the jaw. In his description of the thorax and of the roots of the lungs we would have been glad to see more space given to Bryant's well-devised and well-described operation for their exposure from behind, of which the reader would get no adequate idea from this source. So, too, in dealing with the heart, the author speaks of wounds of its various parts and of the possibility of their treatment by operation, but gives no description of any method by which the heart can be exposed for the purpose. Considering the richness of his advice in most other instances, this would appear to be a distinct omission. In speaking of the abdomen, a section of great value is that dealing with "Operations and Incisions," and here the author is as full as could be desired. This is true also of hernia operations, where the question is asked, How are we to recognize the different hernial layers? and then answered in a very satisfactory way; the author replying that it is neither necessary nor always possible to distinguish all of them, but showing how those which are distinct can be identified. In the surgical anatomy of the lumbar region are found some excellent data concerning psoas and iliac abscesses, it being shown that there are at least two well-marked forms of the latter.

As would be expected, the anatomy and the relations of the appendix are well discussed with the single exception above noted. An example of the minuteness with which particular points are treated may be found in the paragraph devoted to the nerves of the liver, where is furnished an explanation for the occurrence of pain over the right shoulder in certain cases of hepatic disease. The section on the pancreas is disappointingly short. Surely, its surgery has now attained sufficient importance to justify a more complete description of the methods of approach and of affecting posterior drainage. He who would acquaint himself with this subject would turn in vain to this work for that which he should find there. The explanation of retroperitoneal hernia is very good and more succinct than can be found in the same space in any other work with which we are familiar.

And so one might go through this book, finding no fault except here and there where it fails to contain something which the reader might expect to find in it; but it is a book of remarkable merit, showing not merely a large amount of research, but the happy faculty of giving to each anatomical fact its value when applied in practice. The work is sufficiently though not luxuriously illustrated.

Most of the illustrations have been furnished by French works more or less familiar to American students. They are probably just as good as any which might have been made from original sources; they seem, however, to detract from the distinctly American character of the work. We are pleased to see that Dr. Woolsey has abandoned the old expression lymph glands, and adopted the only term which should ever be used—*i. e.*, lymph nodes. The term gland applied to these structures has always been misleading, and implies a primary conception of their function which is quite inaccurate.

The value of the work could be much enhanced by a more complete index. For instance, we find on Plate IX., p. 124, an allusion to the glands of Webber and Blandin, of which we fail to find any description in the text, and to which there is no reference in the index. If they are worthy of mention in the plate they certainly deserve some allusion elsewhere. In spite of these trifling failures or faults, the mention of which might almost be considered captious criticism, we have formed a very high estimate of the value of the work, which we believe to be of very great value alike to general practitioners and to specialists.

R. P.

A Guide to the Practical Examination of Urine, for the Use of Physicians and Students. By James Tyson, M.D. Tenth edition, revised and corrected, with a colored plate and wood engravings. Philadelphia: P. Blakiston's Son & Co., 1902.

The present is the tenth edition of this excellent little manual, and, although new matter has been added, the book has been so revised that its size is not greatly altered. The introduction treats of the technique of urine examination and the general physical and chemical characters of urine. The necessary apparatus for these determinations is described, and all the important chemical tests, together with the reagents used, clearly and concisely given. Part II. deals with the urinary sediments. The text is fully illustrated by woodcuts, both organized and unorganized sediments being adequately pictured. In Part III. methods for the determination of urinary calculi are given, and in an appendix most useful tables are added for reducing the metric system into the English, and *vice versa*. Altogether, the book forms a most excellent guide to the subject of urinalysis, and is especially adapted to those wishing a practical knowledge of urine examination from a clinical standpoint.

W. T. L.

The Elements of Bacteriological Technique: A Laboratory Guide for the Medical, Dental, and Technical Student. By J. W. H. Eyre, M.D., F.R.S. Edin., with 170 illustrations. Philadelphia and London: W. B. Saunders & Co., 1902.

With the general adoption of bacteriological investigation as an aid to diagnosis in clinical medicine, and the widespread use of bacteriology in various branches of industry, there results a definite need for a book devoted exclusively to the technique of this side of scientific work. The present book is not especially intended for the student of medicine, but deals with the methods of bacteriological investigation from a much broader aspect than is to be found in the usual text-books on pathological technique. Indeed, only a very small portion of the volume is allotted to the study of pathogenic bacteria, and thus the work is adapted for use in the dairy or brewery as well as in the pathological laboratory. The first portion includes detailed descriptions of the necessary glass apparatus, microscopes, incubators, the principles of sterilization, and general examination of bacteria and other micro-fungi.

Bacterial stains and the preparation of nutrient media are fully

recounted, and one chapter is devoted to the identification of bacteria, including both physiological and chemical examinations. A classification of fungi, with a description of the anatomy and physiology of the schizomycetes, is a useful addition. At times the description of apparatus and their use impresses one as being unnecessarily detailed, although this is scarcely a fault in a book dealing with the elements of a subject. On the other hand, the portion devoted to the study of the pathogenic bacteria only suggests certain lines of investigation, and would be of little avail to one unfamiliar with the subject.

It is also to be regretted that some of the special media recently devised for the identification of the typhoid bacillus have been omitted, especially since the separation of the colon bacillus from the typhoid bacillus is dwelt on at some length in the chapter on Water-examination. Altogether the book is valuable, since it comprises the standard and most useful method of general bacteriological investigations. The volume numbers something over 350 pages, and contains numerous cuts which amply illustrate the text. W. T. L.

Anleitung zur Diagnose und Therapie der Kehlkoph-, Nasen-, und Ohrenkrankheiten. Vorlesungen gehalten in Fortbildungscursen für practische Aerzte, von Dr. Richard Kayser, in Breslau. Berlin: Verlag Von S. Karger, 1903.

This little book of 170 pages is one of the most practical guides to diagnosis and treatment of the more ordinary pathological conditions met with in the nose, throat, and ear which it has been our pleasure to read. It is intended for the use of the student, the general practitioner, and the beginner in the specialties with which it deals, and within these limits it is a very complete exposition of them. Its author is to be congratulated upon the wisdom with which he has pointed out those conditions which may be properly treated by the tyro as distinguished from those which require special skill in their management. The illustrations are well chosen, accurate, and graphic. F. R. P.

The Mattison Method in Morphinism. By T. B. Mattison, M.D., Medical Director, Brooklyn Home for Narcotic Inebriates. Pp. vi., 40. New York: E. B. Treat & Co., 1902.

A physician who can sum up the results of thirty years' experience in less than forty pages should attract our attention. In this little book he presents a modern and humane treatment of the morphine disease, consisting in preliminary sedation by sodium bromide, rapid deprivation of the drug, meeting the reflex symptoms mainly with codeine, combating the insomnia by trional, and making use of various agencies for the relief of disquieting symptoms. The book is a strong plea for humane treatment, safeguarded against deception and likelihood of relapse, written in a popular style; also, at the same time, sufficiently explicit for the practitioner having the facilities to successfully follow.
R. W. W.

PROGRESS

OF

MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF

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Metabolism in Albuminuria.—EMERSON (*The Johns Hopkins Hospital Reports*, vol. x. p. 323) has made a very careful study of the disturbances of metabolism in a preliminary series of ten cases of nephritis in the medical wards of the Johns Hopkins Hospital. The work was undertaken with the view of determining, if possible, some of the influences governing the amount of albumin in the urine of these cases. The albumin and nitrogen excretion in the urine were specially studied. The former was estimated gravimetrically, and the latter by the Kjeldahl method. Some of the cases are illustrated by charts, indicating the curves representing the total urine, albumin, nitrogen, and temperature lines. His conclusions, with some additional details, are as follows:

1. The percentage of albumin is the best index for the course of a case of albuminuria.

2. In many cases of chronic nephritis there is an acute process in progress, and it is this latter which governs the course of the disease. Variations in the course of this acute process are shown by (*a*) increase in albumin per cent.; (*b*) slight rises in temperature.

3. The effect of various diets, therapeutic measures, muscular work, etc., on the albuminuria is often produced by their effect on this acute process.

4. In governing the diet in nephritis, slight rises in temperature should be taken as evidence that the diet is unsuited to the case.

5. While the acute process is active, milk is the best diet; not too much, and properly diluted. After the acute process has subsided, the patient may even benefit from additions of bread and butter, rice, fruit, or even, later, of meat.

6. If the day and night urines be studied separately, it was found that (*a*) the line of water excretion for the day is practically parallel to that of the

night; but the changes in the night preceding gives the curves the appearance of being the reverse of each other; (*b*) the albumin per cent. of day urine is practically always above that of the night; (*c*) in the night urine the albumin and nitrogen lines are practically parallel, showing some definite relation between the excretion of these, and the percentage of each varies inversely as the amount of urine to a certain degree.

Under normal conditions the kidneys, as well as the other organs, rest somewhat during the night. Quincke, Iljisch, and Laspeyres drew attention to some interesting changes occurring in disease. Iljisch found that in liver, kidney, and heart diseases which produce œdema, the urine voided per hour during the night contains more solids and is greater in amount than that during the day. In renal diseases, even though no œdema be present, the above is true. Laspeyres studied this point in a good many heart, renal, and other diseases. It was confirmed in certain cases of nephritis. He found it true in certain cases with cardiac or arterial disease, and in acute nephritis or chronic parenchymatous nephritis without heart lesion, the normal ratio obtained. He considers, therefore, that this abnormal ratio depends on the organic circulatory disease, and not on the renal condition alone. His explanation is essentially that of Quincke's, that during the night the kidneys have a chance to excrete the fluid of which during the day the tissues could not rid themselves owing to the circulatory disturbances.

On the Micrococcus of Acute Rheumatism.—E. W. Ainley Walker (*The Practitioner*, February, 1903, p. 185) advances bacteriological evidence which, with that of other investigators previously published, tends to strongly support the view that there is a specific organism that causes rheumatic fever.

Of the various organisms that have been isolated in cases of rheumatic fever, staphylococci and streptococci were the ones that were most frequently isolated by the earliest investigators. Achalme isolated a bacillus which gave positive results in experiments on animals. Recently much attention has been directed to an organism which was described by Apert and Triboulet in 1898, but which is, possibly, identical with that isolated by Popoff in 1887. Poynton and Paine have, up to the present time, obtained this diplococcus, as they prefer to consider it, from eighteen cases of acute rheumatism, and have by its inoculation into animals produced polyarthritis, pericarditis, myocarditis, endocarditis, pleurisy, nodule-formation, fungating endocarditis with visceral infarctions, and probably chorea. Fritz Meyer has supported their results in Germany. Poynton and Paine regarded this organism as the specific cause of acute rheumatism, and called it the diplococcus rheumaticus.

Walker and Beaton took up the bacteriological investigation of rheumatic fever, and they have come to the conclusion previously expressed by Poynton and Payne, that a particular micro-organism, and no other, is constantly associated with acute rheumatic lesions. They have isolated this micro-organism in fifteen rheumatic patients. These comprised eight cases of acute rheumatism, three cases of chorea in children, and four of malignant endocarditis in rheumatic subjects. By inoculation of the organism into rabbits they have produced the following effects: acute septicæmia, pericarditis, endocarditis with beady vegetations, pleurisy, and monarthritis or polyarthritis. The

organism has been found in pure culture in the blood, in all the lesions, and in the urine of inoculated animals. Although Poynton and Paine admitted that their organism sometimes formed chains, yet they preferred to call it a diplococcus. Walker and Beaton, however, rather regard it as a form of streptococcus, and suggest micrococcus rheumaticus as a more suitable name for it.

Is rheumatism a manifestation of an attenuated streptococcus septicæmia, as Gustav Singer strongly holds, or is it due to a specific organism? Walker and Beaton, while admitting that it has not yet been definitely established, support the latter view. Specificity, they say, can only be established by the eventual discovery of some characteristic difference, either in the micro-organism or its products, sufficient to distinguish it with certainty from the other members of the "streptococcus" group. They have found some proof to support the view that the organism is a specific one. Marmorek claimed to have proved the identity of all streptococci in man—with the possible exception of that of scarlet fever—by the observation that they all refuse to grow in filtered culture-fluid in which streptococcus has been previously grown and filtered out, although other organisms can grow in such media. Walker and Beaton tested two cultures of their micrococcus rheumaticus by the application of this method, and found abundant growth occurring in the inoculated fluids. They feel that the bacteriological study of rheumatic fever has now reached the stage when some hope of securing a curative serum may reasonably hold out.

SURGERY.

UNDER THE CHARGE OF

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On Four Cases of Perforating Gastric Ulcer, of which Three Recovered.—Jones (*British Medical Journal*, November 29, 1902), after reporting his cases in detail, states that the first case was as simple as the second was complex. A fairly movable ulcer, localized extravasation, and immediate operation were enough to ensure success. The second case, which died, was under chloroform for fifty minutes in consequence of adhesions which had to be separated and the involvement of the cardiac end, the fixation of which rendered suturing a matter of considerable difficulty. This patient died on the fourteenth day after the operation, and at the autopsy a large abscess cavity was found near the posterior portion of the under surface of

the diaphragm. There was a perforation through the diaphragm and into the left lung. Further examination showed the ulcer to be completely healed. Both the last cases were very encouraging, the third inasmuch as operation was not performed until fourteen hours after the rupture had occurred. Although leakage had occurred in the last case, the stomach contents did not appear to be of a very irritating kind. A subphrenic abscess is often found in those cases where the perforation is of the anterior wall of the stomach, and this may be accounted for in either one of two ways: 1. By direct trickling of septic material through the foramen of Winston. 2. By lymphatic absorption. In regard to operative technique, it is well in all cases to scrape the surfaces and edges of the ulcer, and when practical to use a purse-string suture as a preliminary measure. This can be done in a few seconds and all extravasation stopped while the final occlusion is completed. Dry dabs should supersede irrigation, which serves to dilute, disseminate, and make more soluble the toxic contents. As Turner has suggested, one can easily infect the lesser peritoneal cavity by irrigation of the greater. Tobin has stated that no case of perforated gastric ulcer should be removed from where the union has occurred, for any motion simply aids in the escape of the stomach contents into the peritoneal cavity.

Operations for Gastric Ulcer, Acute and Chronic.—PARKER (*British Medical Journal*, November 29, 1902) states that he operated on five cases of chronic ulceration with sudden perforation, with the result that four made a complete recovery, and one died thirteen and one-half hours after operation. In a second series of four cases of chronic ulceration with slow perforation, or, in other words, when the chronic ulceration was attended with a destructive process, but without extravasation, two died and two recovered. In the fatal cases the stitches in each case gave way on the fifth day after the operation. In one case exhaustion was the cause of death, while in the other it was due to a purulent peritonitis.

A Clinical Lecture on Some Cases Simulating Acute Appendicitis.—BARKER (*British Medical Journal*, February 28, 1903) states that the conditions closely simulating appendicitis are: (1) ruptured pyosalpinx; (2) ovarian cyst strangled by twisted pedicle; (3) twist and strangulation of omentum; (4) perforated gastric ulcer; (5) retrocæcal hernia; (6) broken-down caseating glands; (7) ileocæcal cancer, with abscess; (8) hæmatoma of broad ligament; (9) reduction of hernia en masse; (10) intussusception. Ovarian cyst, strangled by a twisted pedicle, may present typical symptoms of the acute form of appendicitis. In fact, in two such cases under the author's care the correct diagnosis was only made after the abdomen was opened. In a recent case of twist and strangulation of the omentum the patient gave a history and presented symptoms wonderfully like those of acute appendicitis—onset, with sudden pain in the right groin, vomiting, abdominal distention, a tender lump above Poupart's ligament, and elevation of temperature. The diagnosis was only made on operation, which exposed the real cause of the trouble. In one case a perforated gastric ulcer gave the symptoms of appendicitis: Sudden onset of pain in the right iliac fossa, which later became general throughout the abdomen. Tenderness and

rigidity of the abdominal walls, slight absence of resonance in the right flank, vomiting, and a rise of temperature to 100° F. There was no shock. The patient also had a reducible right inguinal hernia, which she had reduced on getting into bed, and the first thought was that it had gone back en masse, but there were no definite symptoms. Laparotomy settled the diagnosis, and the patient made a rapid recovery. In one case a retrocæcal hernia closely simulated appendicitis, but the operation showed a gangrenous intestine and general peritonitis, which was soon followed by death. Broken-down caseating glands in the right iliac fossa simulating a subacute appendicitis is not an uncommon condition. In one such case the temperature was up and down; there was a diffused swelling in the right iliac fossa, which was not very painful. On operation a chain of caseating glands running from the cæcum through the mesentery was found and removed and the patient recovered. Although ileocæcal carcinoma with abscess is an uncommon condition in one case of the author's, there was a ring of cancer in the valve, a perforation and resulting abscess, and so all the symptoms of appendicitis. More rarely hæmatoma of the broad ligament, reduction of a hernia en masse, and intussusception may simulate appendicitis, but in the last condition the differential diagnosis should be comparatively easy.

Hydatid Costal Cysts.—Géraud and Mignot (*Revue de Chir.*, No. 1, 1903), after reporting in detail the results of operation in one case, state that the hydatid cysts of bone during a long period of their evolution are of small size and remain latent. It is not the same when they have destroyed a portion of the bone or have extended to the outside. They then present two important symptoms: the spontaneous breaking of the tumor and swelling. This breaking is the result of any insignificant traumatism during any sudden movement, and is often the first symptom revealing the presence of the hydatid disease. More frequently, however, it is the swelling which first attracts the attention. This swelling is smooth, hard, or of unequal consistence, often giving the sensation of parchment crepitation; soft, depressible, presenting rarely the special fremitus, when the hydatids have extended out of the bone and are spread throughout the neighboring soft tissues. Occasionally this tumor is reducible in the interior of the bone; occasionally also when compressed alternately by both hands the two extremities often may give to the contents a movement of coming and going, due to the passage of the mass under a point of bone, as was noticed in the author's case. As the tumor grows it encroaches upon the skin, which is susceptible of being infected, and then abscess formation, which either opens spontaneously or demands an incision for its relief. These infections are very serious and perhaps fatal, and are often the result of an infection developing in a bone affected with cystic degeneration. The phenomena due to the compression of the nerve trunks of the brain or the cord may add to the symptoms those of neuralgia, paraplegia, or the symptoms of a brain tumor, but they present no special characteristics other than those appertaining to all tumors of the bones, the brain, or the spine. One very rarely makes the diagnosis of hydatid bone cyst, and more often the condition is unperceived until the spontaneous fracture of the affected bone attracts the attention. Then one should also think that the spontaneous fracture may be due to tabes, gummatous

osteomyelitis, or sarcoma. The fracture due to tabes is so recognized by the other signs of this condition, the gummatous osteomyelitis by the history of syphilis, the osteocopic pains, and, contrary to the hydatid disease, recovery will follow immobilization, the sarcoma develops rapidly, is accompanied by local heat, by a subcutaneous network of veins more developed than on the opposite side, and sometimes by the movement of pulsation when the tumor is very vascular. Outside of this accident the affection is marked by a swelling of slow and torpid evolution, and should be differentiated from osteosarcoma, and, above all, from tubercular osteitis, which present a clinical picture closely resembling that of the hydatid cyst of bone. However, the tension of the tumor produced by the first affection is much less than that of the second, which gives the sensation of a very stiff and resistant packet. It is certain that the diagnosis is very difficult, and that one is more apt to make the diagnosis of a cold tubercular abscess than that of hydatid cyst. The best method of diagnosis is by capillary puncture or incision, which has the advantage of being provided for at the first for a radical operation. The treatment is surgical, for the indication is to remove all of the hydatid vesicles without their breaking, and so prevent a secondary infection. One difficulty that may present itself is the difficulty of evacuation in those cases where the medullary canal of a long bone or the body of a vertebra is involved. In order to facilitate this search and so absolutely clear out the region infected with the vesicles, it is necessary to make a long incision and then trephine the affected bone and then to hollow out until healthy bone is reached. All the infected bone should be removed either with a gouge or a curette, and then the resulting cavity thoroughly sponged out with salt solution and sterile pads. The depression which results from this loss of substance should be drained, and if suppuration has taken place in the cysts the wound should be left freely open, as after trephining for osteomyelitis. In the case of hydatid cysts which develop in a rib, the indication is to do a partial resection of the bone, as was done in the author's case, care being taken to go wide of the area of disease. If one does not resect enough, one invites a return of the condition. The same operative measures are indicated for the lesions of the bones of the members, lesions which otherwise necessitate amputation, particularly in the case of the lower limb.

A Simple Method of Operating on Piles.—MITCHELL (*British Medical Journal*, February 28, 1903) states that he has used this method with success during the past four years. The technique consists in dilatation of the sphincter, which will bring the piles fully into view, and then the mucous membrane is sponged with a 1:1000 solution of bichloride of mercury. A pile is then clamped in a long, narrow-bladed forceps, such as Kocher's artery forceps. The redundant mucous membrane and pile are cut away with scissors. A curved needle, threaded with catgut that has been hardened in formalin, is then inserted immediately above the clamp and the end of the catgut secured by a knot. A continuous suture is rapidly applied around the clamp, which is then withdrawn and the suture tightened, leaving a vertical line of continuous suture within the rectum. Each pile is similarly treated in turn. The advantages of this method are its rapidity and the lack of bleeding. The suture being continuous is an efficient hæmo-

static. After the forceps are withdrawn it cannot possibly slip, so there is no danger of secondary hemorrhage; no raw surfaces being left, the bowels are encouraged to act regularly from the first. As a rule, patients are able to be up in about a week. The catgut, being absorbed in eight or ten days, does not require removal.

THERAPEUTICS

UNDER THE CHARGE OF

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Intravascular Antisepsis.—DR. J. M. FORTESQUE-BRICKDALE gives the results of a number of experiments conducted at the Jenner Institute of Preventive Medicine. In planning the experiments he had two objects in view: first, to test the toxicity of various antiseptics when injected into the veins of rabbits, and, second, to discover if any of them exerted any influence on the course of an artificially induced septicæmia. In the first series the following substances were chosen: mercury perchloride, mercury oxycyanide, formaldehyde, chinosol, a mixture of formaldehyde and chinosol, protargol, and sodium taurocholate. The conclusions he drew from this series of experiments were: (1) mercury perchloride, mercury oxycyanide, and protargol cannot be injected intravenously into rabbits in sufficient strength to produce an antiseptic effect lasting over several days; (2) that a mixture of chinosol and formaldehyde is too toxic, even in minute doses, to be of use for practical purposes; (3) that chinosol or formaldehyde can be injected intravenously so as to produce a solution which would have an inhibitory action *in vitro;* (4) that sodium taurocholate can be injected in small doses, but the toxic effects manifest themselves after a few days. In the second series made to determine the effect of these antiseptic solutions on anthrax infection, the following conclusions were drawn by the author: (1) that rabbits injected daily with non-toxic doses of mercury oxycyanide, formaldehyde, chinosol, protargol, or mercury perchloride are not thereby protected from the usual effects of previous inoculations of virulent anthrax; and (2) that chinosol and formaldehyde in large doses so depress rabbits infected with pneumococcus that they die sooner than untreated animals. He concludes that at the present time there is no experimental evidence which would warrant the assumption that the course of septicæmia in animals can be influenced favorably by the intravenous injection of antiseptic substances, and that the only result to be obtained by pressing such treatment beyond the maximum non-toxic dose is to hasten the death of the animal.—*The Lancet*, 1903, No. 4141, p. 98.

The Treatment of Typhoid Fever by Acetozone.—Dr. F. G. Harris has tried this remedy in 128 instances of typhoid fever in the Cook County Hospital, taking advantage of a recent epidemic of typhoid, during which at least 600 patients with typhoid fever were admitted to the wards between July 1 and November 1, 1902. The cases were not selected ones and special wards were set apart for giving the acetozone treatment. As is well known, acetozone was first prepared by Novy, and its action is similar to that of hydrogen dioxide, save that it gives off more active oxygen than the former compound; but while giving off more active oxygen, it does not do so with the same violence and rapidity as is observed with hydrogen dioxide. This drug was administered in solution which contained 12 to 15 grains of the powdered acetozone to a quart of hot water. This is placed in a bottle which is stoppered and vigorously shaken from three to five minutes. It is then set aside to cool, and is kept in the form of one-half-gallon bottles in a refrigerator. The solution is used to replace water and all other liquids except milk, which is practically the entire food used during the persistence of the fever. The patients are urged to drink it *ad libitum*. Moreover, 6-ounce doses of this solution are given every four to six hours during the course of the fever. Apart from small doses of sodium phosphate or potassium sulphate to move the bowels, this was the only medication. Temperatures above 102° F. were treated by sponging with cold water. In conclusion, the author stated that many patients were given acetozone very irregularly on account of several contributory causes: dislike of the taste and odor of the solution; resistance of ignorant patients; lack of assistance on the part of overworked attendants, due to the crowded wards caused by the epidemic. Those patients who are given the drug early, often, and regularly show the best results of this treatment. What Virchow calls the "brutal force of figures" cannot but convince anyone but that acetozone lowers the temperature, shortens the duration of the fever, and lessens its toxic symptoms more than our better known treatments. From the information gained in watching this series of 128 instances of typhoid fever, he believes that where patients can be seen during the first week of the illness and given large amounts of acetozone solution regularly and often, assisted by a gentle laxative, the temperature will return to the normal in from ten to twelve days.—*Therapeutic Gazette*, 1903, No. 3, p. 145.

Disodic-methyl-arsenate.—Dr. Thomas R. Fraser contributes a critical paper on this new, much-lauded cacodylate. In a previous communication he had said that the therapeutic effects of arsenic were caused by its pharmacological action, and if arsenic were united with other bodies so as to be incapable of producing any pharmacological action, or of inducing excessive quantities of toxic effects that represent an extreme degree of pharmacological action, it could no longer be capable of producing the therapeutic effects in the disease which are the recognized effects of arsenic. If, therefore, any compound of arsenic, such as the methyl-arsenates or cacodylates, are found to be so inert that they may be administered without producing—in doses considerably above the minimum lethal of the ordinary active compounds of arsenic—any symptoms of the action of arsenic, it must be because the arsenic ion has been rendered inert, and probably because in

the inert compound the arsenic had formed so firm and stable a union with other ingredients of the compound that no dissociating influence to which it is subjected in the body is able to set free the active arsenic compound or ion from the combination. He showed that in the case of the cacodylates large and even enormous doses may be received by human beings without the manifestation of any toxic symptoms whatever, or of only slight toxic symptoms of arsenical poisoning. It was also shown that in several diseases in which the older arsenical compounds are administered with advantage no therapeutic results assignable to arsenic were obtained; and, further, that when cacodylates are administered they pass through the body and are eliminated in such stable combination with organic bodies that they fail to react to the usual tests for arsenates, and fail to yield arsenium when subjected to the dissociating influence of Marsh's process. Further experience of the cacodylates has also shown that, especially when given in large doses by stomach administration, they frequently cause inconvenient effects, such as a disagreeably alliaceous odor of the breath and skin, gastric disorders, and even congestion of the kidneys, which have been attributed to cacodylic oxide, or binoxide, or to sulpho-cacodylates being generated in certain conditions. These bodies are organic compounds of arsenic and methyl, having a special and distinctive action, which, however, is not the action produced by the ordinary compounds of arsenic and well recognized as that of the arsenic ion in these compounds. To obviate these inconveniences, Gautier has recently introduced another organic compound of arsenic, disodic-methyl-arsenate, $AsCH_3O_3Na_2H_2O$, as a substitute for the cacodylates or di-methyl arsenates. He claims for this salt that while it is non-toxic, it possesses the therapeutic potency of arsenic, and that it has an advantage over cacodylates in so far that it may be used not only by subcutaneous or intramuscular injection, but also by stomach administration, without producing the inconveniences or disorders produced by the generation of minute quantities of cacodyloxide or binoxide. To prevent confusion from the similarity of the chemical names of these two and other methyl compounds, Gautier has introduced the name arrhenal for the disodic-methyl-arsenate. This arrhenal is a colorless, crystalline salt, easily dissolved by water and alcohol, non-hygroscopic, and alkaline in taste and reaction. Silver nitrate causes a white and not a yellow or brick-red precipitate in its solutions, thus failing to produce the reaction of an arsenate or arsenite, although it contains 34.5 per cent. of its weight of arsenium, representing 45.5 per cent. of arsenious acid. It is given in doses varying from 3 grains to 0.38 grain daily. It is claimed to have produced good results in tuberculosis, bronchitis, chorea, syphilis, anæmia and pernicious anæmia, adenitis, leukæmia, influenza, and the vomiting of pregnancy, and it is even stated to have established for itself the position of being the most efficient of all remedies for malaria. The enthusiastic praise of this recently introduced organic preparation of so-called latent arsenic, and the diversity of results in its therapeutic applications, appear to justify an examination similar to that which had previously been made of cacodylates. The general results of the operations that have been brought forward are, that the much-praised disodic-methyl-arsenate, or arrhenal, though containing much arsenic, is practically an inert substance; that, even in enormous quantities, it is incapable of pro-

ducing the well-defined pharmacological action and the well-recognized toxic effects of the arsenic ion; and that, as might in that case confidently be anticipated, it is also incapable of exerting the remedial or therapeutic influences which are those of the older and commonly-used compounds of arsenic.—*The Scottish Medical and Surgical Journal*, 1903, vol. xii. p. 193.

OBSTETRICS.

UNDER THE CHARGE OF

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Bossi's Dilator and Eclampsia.—In the *British Medical Journal*, February 21, 1903, BALLANTYNE reports three cases of eclampsia in which he used Bossi's dilator with great satisfaction.

His first case was that of a primipara, aged twenty-three years, in whom there was posterior rotation of the occiput with a large child. Dilatation was obtained in twenty minutes, followed by craniotomy. The mother made an uninterrupted recovery, and the instrument worked with great satisfaction. His second case was that of a woman in her fourth labor, the os being partly dilated, but labor completely arrested. Dilatation required half an hour in this case, followed by the use of forceps, mother and child making a good recovery. His third patient was a primipara, aged twenty-four years, six and a half months advanced in pregnancy, with very rigid cervix, the os very little open. Dilatation in thirty-five minutes was brought to a little over three inches in diameter. He reports no serious injury following the use of this instrument.

Zangemeister (*Centralblatt für Gynäkologie*, No. 4, 1903) reviews the question of the use of Bossi's dilator in eclampsia, and also the various modifications of this instrument which have been made. He believes that great danger of extensive laceration accompanies the use of this instrument. Personally he has used the original instrument of Bossi, and has taken every precaution to dilate the cervix slowly to avoid laceration. In a fatal case of eclampsia he had the opportunity of examining the uterus, and found two long lacerations of the cervix extending to the peritoneum. He was surprised to find how little force was necessary to turn the dilating mechanism, but he considers this one of the dangerous things about the instrument. He points to the danger of septic infection following laceration of the cervix, in addition to hemorrhage. Personally he much prefers the use of elastic dilators.

Hyperpyrexia with Thrombosis of the Inferior Vena Cava.—FOTHERGILL (*British Medical Journal*, March 7, 1903) reports the case of a patient

delivered by a midwife who had high fever. Retention of the placenta had occurred with infection. A temperature of 111.2° F. was observed, reduced somewhat by hot sponging. Immediately after this thrombosis of the right femoral vein followed, and immediately the same condition in the left femoral vein. There were repeated chills, with great changes in temperature. There was no sign of suppuration or embolus in any other organ. Death ensued from œdema of the lungs. On autopsy the inferior vena cava and its tributaries were filled with ante-mortem clot from the heart downward.

Laceration of the Vagina during Labor.—KAUFMAN contributes to the *Archiv für Gynäkologie*, Band 68, Heft 1, 1903, an extensive paper upon this subject, in which he has collected 82 cases of this complication of labor. But only a portion of these were available for statistical study, as many of them were imperfectly reported.

Most of them occurred when the fœtus presented by the vertex, next in frequency in transverse positions, and least often in breech presentations. In 78 cases, 49 happened in spontaneous labor. In 29, some violent effort at extraction had been made. The condition of the pelvis was reported in 58 of these cases. In 38 the pelvis was said to be normal, and in 20 to have been contracted. In 3 cases myoma of the uterus was present as a complication, and in 1 case a divided uterus, and in 1 scars were found in the vagina and adjacent tissue. Almost all of the patients were multiparæ, as the accident happens very rarely in primiparous patients. In a few of these cases the children were of excessive size, although in most they were of ordinary development. In 68 cases the abdominal cavity was opened through the peritoneal sac. In 14 of these the intestine prolapsed, and in 1 case an ovary and tube. In 29 of these cases the child made its way out of the uterus, in 26 into the abdominal cavity, and in 3 into the subperitoneal tissue.

The placenta was found in 30 cases outside the uterus, in 27 cases in the abdominal cavity, and in 3 cases in the tissue beneath the peritoneum.

As regards the method of delivery most apt to result in injury to the vagina, it was found that version and extraction was especially dangerous, next the forceps, next extraction only, while craniotomy was more apt to produce the accident than eventeration or decapitation. Three of these patients died undelivered.

The treatment of the complication may be divided into those cases in which abdominal section, with or without extirpation of the uterus, was practised, and those cases in which the accident was treated by suture or tampon applied through the vagina. Treatment was selected in accordance with the extent of the laceration and the involvement of the uterus. When the uterus was uninjured and the laceration can be reached from the vulva it was closed by suture; and if the uterus was uninjured and the laceration could not well be reached, tampon and drainage with gauze was the method employed.

The mortality was 35 per cent. in cases where both the uterus and vagina were injured, the most frequent cause of death being septic infection, and next in order hemorrhage.

In cases where the vagina only was injured the mortality was 25 per cent. In these cases the mortality from bleeding was but 5 per cent., septic infection playing the more important part.

The symptoms of this accident depend entirely upon the extent of the laceration. A small rupture of the vagina during labor may give rise to no symptom, and may not be discovered until an examination is made after the birth of the child. Some have laid stress upon the contraction of the round ligaments and upon the suffering and anxiety of the patient. Uterine contractions are not always excessive in these cases, and the patient may not complain of excessive suffering. The mortality from hemorrhage is considerable, and depends upon the extension of the laceration into the connective tissue about the uterus.

In diagnosing the condition, examination by the introduction of the entire hand is necessary to accurately localize the injury.

So far as the prognosis is concerned, the mortality of rupture of the uterus as variously stated at present is from 60 to 73 per cent. The mortality of rupture of the vagina is much less, and may be reckoned at 25 per cent., as has been stated, in favorable and uncomplicated cases.

The prognosis for the children is exceedingly bad in cases of vaginal rupture. The placenta is almost invariably prematurely separated in these cases, and as a consequence the fœtus rapidly perishes. The prognosis for the child is so bad that its interests must not be considered in selecting a method of treatment.

In the treatment of these cases, if laceration happens before the termination of labor, the patient must be delivered as rapidly as possible, no attention being paid to the life of the child; hence, craniotomy or any other method of delivery which will subject the mother to the least violence should be chosen. Perforation of the after-coming head should be employed if the slightest difficulty arises in its delivery. Usually the forceps can be employed to advantage when the head is presenting.

Double Pregnancy in Double Uterus.—In the *British Medical Journal*, March 7, 1903, HELLIER reports the case of a patient, aged thirty-four years, who had had three normal labors previously. During the fourth pregnancy the uterus was larger than usual. After normal labor spontaneous expulsion of a female child occurred by the usual mechanism, its placenta following. It was found that a second child was present, but the physician in attendance, on introducing his hand, found the uterus empty. A second os was discovered high in the pelvis, in front of and to the left of the first. A double uterus was present, and in this second half was a male child, which was delivered by podalic version. The partition between the two halves of the uterus was distinct and quite thick.

Fœtal Ascites.—EDEN reports a case of this comparatively rare condition in the *British Medical Journal*, February 21, 1903. The patient was an unmarried primipara, aged eighteen years, in labor with a footling presentation. The pregnancy was about the end of the eighth month. Labor was very slow; the child died and became macerated. Efforts were made to deliver the fœtus by traction upon the feet. Each traction brought away a

piece of the child until the attending physician could bring away no more. On careful examination it was found that some pathological condition in the abdomen of the fœtus prevented its complete delivery. The abdomen was opened with scissors and several quarts of thin yellowish fluid escaped. The child was then readily delivered. The placenta was adherent, and had to be removed manually. On examining the body of the fœtus the peritoneal cavity was enormously distended, and there were no peritoneal adhesions. The bladder was distended moderately and the urethra was impervious.

GYNECOLOGY.

UNDER THE CHARGE OF

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ASSISTED BY

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Progressive Peritonitis.—KREEKE (*Zentralblatt für Gynäkologie*, 1903, No. 7) calls attention to the fact that diffuse septic peritonitis in its early stage is more or less limited, so that, even when the peritoneal cavity seems to be filled with pus, there is a chance of saving the patient by operation, provided that a fatal degree of absorption is not yet present. The limit is thirty-six hours. The writer has had successful cases ranging from five to twenty-eight hours after the onset of peritonitis.

The pulse and temperature cannot be relied upon as positive indications of the severity of the initial infection; nor is tympanites a constant symptom; in fact, the abdomen may be retracted, but extreme tenderness on palpation is seldom absent.

A free median incision should be made, with lateral incisions if necessary. Though irrigation and drainage are all-important, much depends upon the after-treatment of these cases. Nourishment by mouth is avoided until gas passes freely. Enemata of saline solution relieve thirst, and the heart action is stimulated by intravenous infusion, from one to two pints being given every eight hours. Camphorated oil is a valuable stimulant.

Lavage is indicated for the relief of obstinate vomiting. The bowels should be moved early with salines, administered hypodermically if necessary. If intestinal paralysis cannot be overcome, it may be advisable to establish an artificial anus in the ascending colon. In one of the writer's cases the fistula closed spontaneously in six days. With the reappearance of fever new abscesses should be sought for and drained.

In the discussion of this paper before the Munich Gynecological Society, several speakers referred to the value of full doses of atropine in intestinal paralysis.

[The writer has always insisted that in the majority of the successful

cases of cœliotomy for acute septic peritonitis the inflammation was not diffuse, but was limited to the lower half of the abdominal cavity, and was not attended by the systemic infection which is invariably fatal. All cases of more than thirty-six hours' standing are doubtless of this circumscribed character. The writer is able to add a recent successful case in which the operation was performed at the onset of the symptoms, the only indications being, as the writer has stated, general abdominal tenderness and muscular rigidity, without elevation of temperature; in fact, the condition was supposed to be ruptured ectopic.—H. C. C.]

Phenomena following Removal of the Adnexa.—WITSCHEL (*Zentralblatt für Gynäkologie*, 1903, No. 7) tabulates 138 cases from the Strasburg Clinic, in which he notes the fact that there is a marked diminution in the post-operative disturbances following hysterectomy in cases in which the ovaries are preserved. Psychoses were absent. Menstrual molimina were noted more frequently in the latter cases.

Sexual desire persisted in over 50 per cent., whether the ovaries were removed or not, and there was no difference as regarded mental confusion.

Adenoma Malignum in a Young Woman.—URBAN (*Zentralblatt für Gynäkologie*, 1903, No. 7) reports the case of a girl, aged twenty-one years, whose uterus was removed for obstinate hemorrhage. The writer refuses to admit that true adenoma of the uterus is ever a benign neoplasm. He believes that the condition described as adenoma benignum is either glandular polypus or simple glandular endometritis.

Results of Alexander's Operation.—WIELAND (*Zentralblatt für Gynäkologie*, 1903, No. 7) reports thirty-two cases from the Griefswald Clinic, in which subsequent disturbances were noted in only five, such as vesical irritation, dysmenorrhœa, and pain in the cicatrices. Hernia occurred in a single instance; twenty-three patients subsequently became pregnant, eleven being relieved spontaneously, one instrumentally, while seven women aborted. In seven cases (!) the ligaments were torn asunder while making traction upon them.

Venous Stasis as a Cause of Retro-uterine Hæmatocele.—BÜRKLE (*Zentralblatt für Gynäkologie*, 1903, No. 7) believes that hæmatocele is due to general hyperæmia more frequently than is usually supposed, as proved by fourteen autopsies at the Pathological Institute in Prague. He instances the case of a woman, with no history of previous pelvic trouble, who had a severe attack of pneumonia three weeks after her last menstrual period. She suddenly developed tympanites, associated with pain in the lower abdomen, vomiting, diarrhœa, vesical tenesmus, and feeble pulse. A swelling was felt in Douglas' pouch, which was incised per vaginam, and a quart of dark blood was evacuated. The pelvic organs were normal, and careful microscopic examination of the fluid and clotted blood showed no evidence of chorionic structures. The bacteriological examination was negative.

The writer infers that the hemorrhage was a sort of "compensatory or natural venesection."

OPHTHALMOLOGY.

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Subjective Visual Sensations.—URBANTSCHITSCH (*Klin. Therap. Wochen.*, 1902, No. 45) made a series of experiments upon a large number of healthy persons, hysterical and neurasthenic subjects excluded, upon subjective influence on visual sensations. After prolonged fixation of a quiescent, narrow object (a window-sash or a line) the same appears to many persons to become crooked, to waver, or to oscillate. Cross-lines also appear to revolve about their point of intersection (deceptive movements). Individuals inclined to vertigo are especially apt to observe this phenomena in marked degrees. Fixed points also show similar movements—jumping, waving, swaying, oscillating, or revolving Such movements had already been noticed by Humboldt to affect the stars (stellar swayings). Exner explained this as being due to inexact localization of visual impressions. The occurrence of such deceptive movements is furthered by various stimuli (tactile, thermic, electric, acoustic), whereby a different movement—but as it seems constant for the same individual and the same stimulus—corresponds to different stimuli. Such movement, however, is not the same, even to the same stimulus for both eyes. It may thus happen that the movement ceases during binocular vision, and the point is quiescent; whereas, in monocular vision the movements seem to take place in opposite directions for each eye separately, cancelling one another during binocular vision. The movements are called forth even by weak galvanic currents.

While observing a black point many persons notice beside it a false image in the form of a dark disk, a semicircle, a square, etc. This image is normally quiescent. Upon application of the above-mentioned stimuli it is seen to move, changed in form, or perhaps observed only then, and that, too, in a manner characteristic of the particular stimulus, or even of the particular portion of the body which has been stimulated. Such appearances also arise while observing a white surface, if a stimulus is allowed to act upon the observer. Appearance and kind of stimulus stand, as it seems, in the same individual in a constant relation to one another. These appearances are not called forth, modified, or set in motion by actual tones, but rather through an acoustic after-sensation. They may be different upon stimulation of the left auditory apparatus from that of the right.

These subjective movements may be further modified by looking at the object through a colored glass. Upon observing colored lines coincidently with certain stimuli—*e. g.*, a tone—subjective images of characteristically colored lines appear; for example, with deep notes the images are red; with

high notes, green. The form of these subjective images also depends upon the color of the surface upon which they appear. Such an image, if it be looked at through two differently colored glasses (*e. g.*, red before one eye, green before the other), becomes decidedly changed in color through some stimulus, *e. g.*, a tone, passing from red to green, showing a mixture of colors or colored spots. If three differently colored adjacent fields are looked at and a stimulus is made to affect the body, a particular one of the fields, according to the nature of the stimulus—*e. g.*, the pitch of the tone—enlarges, contracts, or even disappears. The color of optical after-images is also changed by various stimuli. In this way a positive after-image may be changed into a negative one; so, likewise, after-images looked at at the same time through two differently colored glasses are changed by stimuli (auditory, gustatory, tactile, etc.); in color they appear mixed or parti-colored. It is an interesting fact that acoustic after-images are able to modify optical images in an analogous manner. When a colored surface is looked at subjective images—*e. g.*, spots, geometrical figures, etc.—appear thereon, determined by various stimuli. It is a strange fact that they may be excited even by the remembrance of a tone. They then correspond to the after-image which arises when the tone is actually heard. A white surface changes, if a colored one is strongly called up in imagination, into that color, and after-images also appear. An after-image already present may be changed in color if that color is called up in imagination. If, while regarding a subjective colored surface another color is thought of, the surface goes over first into a mixture of the two colors, and finally into that of the second. It is possible in this way to mingle objective colors with subjective. An actual red surface appears violet if blue be called up in imagination.

The Cosmetic Value of Paraffin Injections after Enucleation of the Eyeball.—RAMSAY, Glasgow (*Lancet*, January 31, 1903), records his experience in the use of paraffin in 22 cases for forming a stump on which to fit an artificial eye. His method of procedure is as follows: The conjunctiva is divided as close as possible to the corneal margin. Each rectus muscle is caught up on a strabismus hook and sutured to the overlying conjunctiva with a strand of catgut. The tendons of the recti muscles are cut at their insertion into the sclerotic, and thereafter the operation for the removal of the eyeball is completed in the ordinary manner. The capsule of Tenon is packed with gauze till a strong black silk purse suture has been passed around the conjunctival margin, and then, the packing being removed, the melted paraffin is injected with a carefully sterilized glass syringe, the capsule being opened to its utmost capacity by holding the recti muscles on the stretch by means of the four catgut sutures and filled to overflowing. The purse suture is then tightened and securely fixed by a double knot, and the catgut sutures are tied, the superior rectus muscle being approximated to the inferior and the internal to the external.

This operation is followed by very little inflammatory reaction. The purse suture is removed in two weeks, at which time there will be found over the freely-movable paraffin stump a clean, non-discharging surface of conjunctiva. A week later an artificial eye can be adjusted.

To ensure success two points require special attention. First, the operation must be carried out with every precaution against sepsis, and so it must not be attempted in cases where the eyeball is in a state of active suppuration; and, secondly, the sutures must hold the conjunctiva in accurate position over the paraffin. It is important to see that an equal grip is taken of the conjunctiva all around the free edge, and that too wide an interval is not left between the stitches.

There were four failures in Ramsay's 22 cases. In one case after the enucleation of a supporting eyeball pus appeared in the socket and set up so much inflammatory reaction that the stitches were removed and the moulded paraffin allowed to escape. In 3 cases the paraffin came out through inefficiency of the stitching. The 18 remaining cases gave a satisfactory cosmetic result, with free movement of the prothesis.

PATHOLOGY AND BACTERIOLOGY.

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Symposium on Snake Venom: 1. The Poison of Serpents, MITCHELL. 2. Venom and Antivenene, MCFARLAND. 3. A Comparative Study of Snake Venom and Snake Sera, NOGUCHI (*Proceedings of the Pathological Society of Philadelphia*, February, 1903, vol. vi., No. 4).—Mitchell opened this symposium with an interesting historical introduction. Bonaparte had indicated the albuminous character of snake poison in 1843. Mitchell began his researches on snake venom in 1857, and at intervals continued them until 1899, both alone and in connection with Reichert and Stewart. The general toxicity, pathology, and action of venom on the blood were so completely worked out as to leave only a few points undetermined. During the last two years Flexner and Noguchi have worked on snake poison in the light of the recent important theories of immunity inaugurated by Bordet and Ehrlich.

Calmette has succeeded in immunizing horses against cobra poison by heating the venom to 70°, which removed the local irritating poison while not affecting the neurotoxin. McFarland began immunizations with cobra venom on Calmette's principle. On turning his attention to immunization against rattlesnake venom, an extremely irritative local poison made the injection of large animals wellnigh impossible. At the end of a year, however, the horse serum possessed protective powers against the neurotoxic

principle of both cobra and rattlesnake venom and gave precipitates with rattlesnake venom markedly, and with cobra venom to a less extent.

The work of Flexner and Noguchi has been important as confirmatory of Ehrlich's lateral chain theory of immunity. It was found that the various venoms act as an intermediary body to bring about hæmolysis of the blood of susceptible animals in presence of the blood serum, which completes the hæmolysis by its complementing action. In most cases, in the absence of serum, no hæmolysis takes place. Whenever it does, however, the lysis of the corpuscles has been shown by Kyes to be due to an endocomplement within the blood cells. Unmodified snake serum also produces hæmolysis, but when heated to destroy the complement is not hæmolytic, and does not recover complement from the serum of the alien blood, in this respect differing in its action from venom. Venom itself when fresh contains no complement, but is reactivated by snake complement as well as by the complement of susceptible bloods. The serum of animals inoculated with heated rattlesnake serum protects against the hæmolytic action of rattlesnake serum, and the venoms of rattlesnake, cobra, and moccasin.

The Pancreas in Cirrhosis of the Liver.—Steinhaus (*Deut. Arch. f. klin. Med.*, 1902, Bd. 74, p. 537) made a study of the pancreas in twelve cases of cirrhosis of the liver. In all, except one instance, the pancreas showed a more or less grave chronic inflammation. The one exception was a typical case of Laennec's cirrhosis of the liver. The chronic inflammatory changes in the pancreas consisted in a connective tissue growth, which was sometimes of a perilobular type, sometimes of a periacinar type, and although occasionally the parenchyma of the organ was in large part replaced by fibrous tissue, in no case were the islands of Langerhans involved. These structures appeared to be normal in every case. A transient glycosuria was noted in one case, and the author calls attention to the possible relation which may exist between chronic inflammatory lesions of the pancreas and the alimentary glycosuria of cirrhosis of the liver.

Ring Bodies (Nuclear Remnants) in Anæmic Blood.—Cabot (*Journal of Medical Research*, 1903, vol. ix. p. 15), using Wright's modification of Leishmann's stain in studying the blood from cases of anæmia, observed peculiar stained ring formations within certain of the red blood corpuscles. These figures were seen in three cases of pernicious anæmia, four of lead poisoning, and one of lymphatic leukæmia. Unlike the ordinary basophilic granulations found so often in the red blood cells from cases of lead poisoning and pernicious anæmia, these figures stained not blue, but bright red. The rings were quite perfect. They varied in size: in some instances being very small, in others encircling the extreme periphery of the corpuscle. Rarely they were twisted or had a figure-of-eight form. Occasionally basophilic granulations were noted in the same corpuscle which contained a ring body. Such figures did not appear in blood specimens stained with hæmatoxylin. The author believes that they may be connected in some manner with cell regeneration, and suggests that they may represent nuclear remains, or, perhaps, portions of the nucleus which have resisted those forces destructive to it, and ultimately to the cell itself.

HYGIENE AND PUBLIC HEALTH.

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Action of Water on Lead.—Dr. S. Ruzicka (*Archiv für Hygiene*, xli., p. 23) has conducted a series of experiments with distilled water and with solutions of salts of calcium, magnesium, potassium, sodium, and ammonium (sulphates, chlorides, carbonates, and nitrates) on clean lead pipe under various conditions, as contact with air, exclusion of air, renewal of the solutions, mixing of solutions, etc., and has determined the amounts of lead taken up in each case. Water containing carbon dioxide, and solutions containing organic matter from grass, peat, radish leaves, and fish flesh were tried, also. He concludes as follows: 1. The influence of inorganic salts in solution is independent of the nature of the base, but is due wholly to the combined acids. Nitrates in solution cause almost as much corrosion as does distilled water, but chlorides, sulphates, and carbonates exert a restraining action, the intensity of such influence being greatest with the last mentioned. 2. With combined solutions of salts the order of the restraining influence of the several salts is, from least to greatest, nitrates, chlorides, sulphates, carbonates. Carbonates always diminish the rate of corrosion by the other three; sulphates, that by chlorides and nitrates; chlorides, that by sulphates and nitrates; and nitrates always increase the action of the other three. 3. If lead comes continuously in contact with fresh portions of a carbonate solution, the amount of lead given up, small in any event, diminishes progressively. 4. A relatively small amount of carbonate can overcome the influence of nitrate (6 carbonate to 10 nitrate), but when it falls at all below the necessary amount (to 5 parts, for instance), the action increases at once. 5. Free carbon dioxide, contrary to general belief, causes diminished action with both distilled water and the salt solutions. 6. The organic matters of peat increase corrosion; those of the other substances employed inhibit it. 7. Carbonates, carbon dioxide, and extracts of grass and of radish leaves exert greater inhibitive influence than the other substances used. Under all conditions, access of air results in increased corrosion.

The restraining influence of carbon dioxide is testified to also by F. Clowes (*Proceedings of the Chemical Society*, 1902, vol. xviii. p. 46), whose experiments yielded results substantially, but not wholly, in agreement with the above. He found that soluble sulphates and sulphuric acid exert a greater restraining influence than that of the carbonates. Calcium hydroxide in large amounts promotes corrosion. He determined the nature of the compound of lead resulting when pure lead is brought into contact with ordinary distilled water. Considerable lead goes into solution, probably as hydroxide; but, on filtering, a lead compound soluble in cold acetic acid remains on the paper. This

was found to be a hydroxy-carbonate containing three molecules of carbonate and one of hydroxide ($3PbCO_3.PbO_2H_2$). The first reaction with aërated water appears to be oxidation and formation of hydroxide, which then is precipitated by carbon dioxide as basic carbonate.

Disinfection by Dry Heat.—SCHUMBURG (*Zeitschrift für Hygiene und Infectionskrankheiten*, xli. p. 167) shows that, although dry hot air is so uncertain in its action as to be unsuitable for practical disinfection, air at 100° C. will kill the most resistant non-sporing bacteria in and on clothing and other objects within an hour, if it contains from 55 to 65 per cent. relative humidity. This degree of moisture can be attained by having a vessel of water in the space where the objects are treated. Since disinfection of clothing and other objects containing anthrax and tetanus spores is very seldom needed, and since, on the other hand, the bacteria most commonly the object of disinfection (those of typhoid fever, cholera, plague, influenza, diphtheria, tuberculosis, and, probably, measles and scarlet fever, and the pus cocci) form no spores, disinfection with moist hot air will suffice in almost all cases. This method has this advantage over disinfection by steam: that articles of leather (gloves, books, riding breeches, etc.) may be exposed from six to eight hours without injury.

The Neutral-red Method in the Differentiation of B. Coli and B. Typhosus.—A systematic test of a number of races of coli and typhoid organisms with neutral-red has been made by M. P. FITZGERALD and GEORGE DREYER (*Biochemisches Centralblatt*, March 1, 1903, p. 238), who used peptone bouillon and agar containing 0.5 or 1.0 per cent. aqueous solution of neutral-red and varying amounts of acid, alkali, and glucose. They found but one qualitative difference between *B. coli* and *B. typhosus*, and hence, one cannot be satisfied with this one test alone. Glucose-free bouillon is preferable to agar. Large amounts of acid interfere with the reaction, and one must avoid the presence of 0.5 per cent. or more of glucose. The best medium appeared to be 3 per cent. lactose bouillon with the above-mentioned amount of neutral-red. In four to six days, *B. typhosus* gives a yellow color, while *B. coli* gives a red. The original color of the liquid has no influence on the end result. When the typical color once appears it persists. The result is less dependent upon the amount of free acid or alkali than with other methods. Different samples of neutral-red appeared to be reducible in different degrees.

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